# Lipid-lowering Therapy and Goal Achievement in High-risk Patients From French General Practice

Ferrières, Jean; Gorcyca, Katherine; Iorga, Şerban R; Ansell, David; Steen, Dylan L

*DOI:*
10.1016/j.clinthera.2018.07.008

# Lipid-lowering Therapy and Goal Achievement in High-risk Patients from French General Practice

**Jean Ferrières MD, MSc, FESC[a*]; Katherine Gorcyca PharmD[b]; Şerban R. Iorga PhD[c]; David Ansell MD, MRCS, PhD[d]; and Dylan L. Steen MD, MS[e]**

*[a]Department of Cardiology, Toulouse University School of Medicine, Rangueil Hospital, TSA 50032, 31059 Toulouse cedex 9, France. E-mail: jean.ferrieres@univ-tlse3.fr*

*[b]Formerly Sanofi, 55 Corporate Drive, Bridgewater, NJ 08807, USA. Email: gorcycak@gmail.com*

*[c]Regeneron Pharmaceuticals, 777 Old Saw Mill River Road Bldg. #3, Level #3 Room 33-320, Tarrytown, NY 10591, USA. Email: serban.iorga@regeneron.com*

*[d]IQVIA, 210 Pentonville Rd, London N1 9JY, UK. Email: dr.david.ansell@gmail.com*

*[e]University of Cincinnati Medical Center, Medical Science Building, 231 Albert Sabin Way, Rm 3354A, Cincinnati, OH 45221, USA. Email: STEENDL@ucmail.uc.edu*

***Corresponding author:** Dr. Jean Ferrières, Department of Cardiology, Toulouse University School of Medicine, Rangueil Hospital, TSA 50032, 31059 Toulouse cedex 9, France. Phone: +33 5 61 14 59 49. E-mail: jean.ferrieres@univ-tlse3.fr

Abbreviations: ARB = angiotensin II receptor blocker; ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; CHD = coronary heart disease; CHF = coronary heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; EAS = European Atherosclerosis Society; EMR = electronic medical record; ESC = European Society of Cardiology; HAS = Haute Autorité de Santé; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy; MI = myocardial infarction; NICE = National Institute for Health and Care Excellence; PAD = peripheral arterial disease; PCSK9 = proprotein convertase subtilisin/kexin type 9; TIA = transient ischemic attack.

## Conflict of interest statement

JF has received grants and speaker's fees from Amgen, Merck, and Sanofi, and speaker's fees from AstraZeneca. KG was an employee of Sanofi at the time of this study. SRI is an employee of Regeneron Pharmaceuticals, Inc. DA was an employee of IQVIA at the time of this study. DLS has received modest consultant/advisory fees from Sanofi and Regeneron Pharmaceuticals, Inc.

## Acknowledgements

This work was supported by Sanofi and Regeneron Pharmaceuticals, Inc.

Medical writing support under the direction of the authors was provided by Emmanuel Ogunnowo, PhD, of Prime (Knutsford, UK) and Jeff Alexander of SNELL Medical Communication Inc. (Quebec, Canada), supported by Sanofi and Regeneron Pharmaceuticals, Inc., according to Good Publication Practice guidelines (Link). The sponsors were involved in the study design and collection, analysis, and interpretation of data, as well as data checking of information provided in the manuscript. The authors were responsible for all content and editorial decisions and received no honoraria related to the development of this publication.

JF was involved with the design of the study, interpretation of data and critical review of drafts. KG was involved with the design of the study, interpretation of data, and critical review of drafts. SRI was involved with the design of the study, interpretation of data, and critical review of drafts. DA was involved with the design of the study, acquisition, analysis and interpretation of data, and critical review of drafts. DLS was involved with the design of the study, interpretation of data, and critical review of drafts. All authors provided final approval of the submitted manuscript.

**Limits (target journal – *Clinical Therapeutics*)**

Word Count: 3468 (main text including legends to figures and tables; no maximum stated); 400 (abstract)

Tables and Figures: 4 Tables, 1 Figure (no maximum stated)

References: 33 (no maximum stated)

## ABSTRACT

(Word count: 258 [max of 400 allowed])

*Purpose:* To summarize lipid-lowering therapy (LLT) usage patterns and achievement of guideline-identified lipid goals in a 2015 general practice cohort of French patients with atherosclerotic cardiovascular disease (ASCVD) and/or diabetes mellitus (DM).

*Methods:* From the IMS Health Real-World Data database, patients aged ≥18 years were classified hierarchically into mutually exclusive categories of ASCVD subgroups and DM. LLT use and lipid goal achievement were assessed on the date of lipid measurement. The data were compared to previously published results of LLT use and lipid goal achievement in a 2014 UK population.

*Findings:* Of 32,924 patients meeting the inclusion criteria, only 47.5% were prescribed a statin as of the index date. Hierarchically, the highest rates of use of any statin (73.3%) and high-intensity statin (43.3%) were among patients with recent acute coronary syndrome; rates in DM without ASCVD were 38.7% and 2.3%, respectively. Overall, achievement of low-density lipoprotein cholesterol (LDL-C) <1.8 mmol/l (<70 mg/dl) was only 13.9% for patients with ASCVD and 10.7% with DM. Relative to a 2014 UK population, the 2015 French cohort (data re-analyzed according to the UK statin categorization) were prescribed “high-dose statins” less frequently (31.4% vs 20.9%, and 18.7% vs 7.2%, for ASCVD and DM, respectively). Similarly, the proportion of patients with high-dose statins achieving LDL-C <1.8 mmol/l was higher in the 2014 UK than the 2015 French population (37.3% vs 22.2%, and 36.4% vs 20.3%, for ASCVD and DM, respectively).

*Implications:* In a large cohort of French patients with ASCVD and/or DM, LLT usage and LDL-C goal achievement were suboptimal relative to current guidelines.

*Key words:* lipoprotein and hyperlipidemia, coronary artery disease, acute coronary syndrome, cardiac risk factors and prevention

## Highlights

- In this study, 47.5% of French patients with ASCVD or DM received statin therapy
- Only 13.9% with ASCVD and 10.7% with DM achieved LDL-C <1.8 mmol/l
- Fewer French vs UK patients received high-dose statin and reached LDL-C <1.8 mmol/l
- Findings suggest suboptimal statin utilization and LDL-C achievement in France

## Introduction

In France, cardiovascular disease is the second most common cause of mortality after cancer.[1] Across the nation, ischemic heart disease and stroke account for 12% of all deaths.[2] Approximately 80,000–100,000 hospitalizations annually are due to acute coronary syndromes (ACS).[3]

Treatment guidelines for atherogenic cholesterol, the primary modifiable risk factor for adverse atherosclerotic outcomes, include those from the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS)[4] and the French National Authority for Health (Haute Autorité de Santé [HAS]).[5, 6] As of 2006–2007,[7] the vast majority of high-risk patients defined by either guideline had not achieved the recommended low-density lipoprotein cholesterol (LDL-C) goals, largely due to insufficient treatment with lipid-lowering therapy (LLT).[8]

There is a paucity of data on current atherogenic cholesterol management in patients at the highest risk of atherosclerotic events: those with established atherosclerotic cardiovascular disease (ASCVD) and/or diabetes mellitus (DM). The objective of this study was to evaluate utilization of LLT medications as well as LDL-C and non-high-density lipoprotein cholesterol (non-HDL-C) goal achievement in these patients using a 2015 real-world, generalizable French cohort.

# Methods

## Study population

This was a retrospective, cross-sectional, observational study using electronic medical records (EMRs) from the IMS Health Real-World Data database in France (formerly known as the Longitudinal Patient Database) that included 1.85 million patients representing approximately 2.8% of the French population, from 1200 general practitioners in 2015. These secondary data consisted of anonymized observations that had been collected through EMRs completed by French physicians during office visits. The database has been validated and is representative of the French population.[9] In this study, a retrospective analysis was conducted utilizing a secondary database consisting of existing anonymized observations for de-identified patients, there therefore was no requirement to seek specific Ethics Committee approval.

Inclusion criteria were: ≥18 years of age; an LDL-C measurement within a valid range (0.0259–25.86 mmol/l [1–1000 mg/dl]) in 2015; ≥2 years of continuous representation in the database before the index date (defined as the last LDL-C measurement in 2015); and ≥1 high cardiovascular risk condition (conditions defined below). Continuous representation in the database prior to the index date was required to ensure optimal characterization of the cohort, including its demographics and clinical characteristics, as well as prior and current pharmacologic treatment.

Patients with evidence of any of the following categories of conditions during the pre-index period were identified: 1) recent ACS (myocardial infarction [MI] or unstable angina ≤12 months prior to the index date); 2) chronic coronary heart disease (CHD; MI or unstable or stable angina >12 months prior to the index date

and/or history of stable angina, coronary revascularization, or another CHD diagnosis); 3) ischemic stroke/transient ischemic attack (TIA); 4) peripheral arterial disease (PAD; abdominal aortic aneurysm, carotid and intracerebral artery disease without evidence of stroke/TIA, or any revascularization or repair of these arteries); and 5) DM (type 1 or type 2). High cardiovascular risk conditions were identified using French Thesaurus codes mapped to the International Classification of Diseases, Ninth and Tenth Revisions (Supplementary Table I).

Classification was performed using two methods. The first, hierarchical classification, entailed assigning each patient to the highest mutually exclusive category for which he/she qualified (using the order above). The second, prevalent classification, entailed assigning each patient to all the categories for which he/she qualified. Thus, in hierarchical classification, each patient could only be assigned to one category but in prevalent classification, each patient could be classified into more than one category. For this manuscript, results are reported using the hierarchical classification method, while the Supplementary Material include analyses using the prevalent classification method. The first four high cardiovascular risk categories are collectively referred to as “ASCVD” in the paper.

**Determination of LLT**

For any medication, patients were considered to have been treated on the index date if medication supply via a written prescription was available on or within 30 days prior to the index date, regardless of the duration of the prescription. Patients not currently treated, but with evidence of a past prescription, were considered to have a history of treatment. Patients with no recorded prescription during the 2 years prior were considered to have no evidence of treatment (Supplementary Figure 1).

Statins were classified as high-intensity (atorvastatin 40 mg, 80 mg; rosuvastatin 20 mg, 40 mg; and simvastatin 80 mg) or low-to-moderate-intensity (all other statin medications and doses). For patients prescribed statins, the use of concomitant non-statin LLT was evaluated by a hierarchical classification: 1) statin plus ezetimibe; 2) statin plus a fibrate (i.e., gemfibrozil, fenofibrate, ciprofibrate, or bezafibrate); 3) statin plus the bile acid sequestrant cholestyramine; and 4) statin without any of these non-statin LLT medications (termed “statin monotherapy”). For patients prescribed only non-statin LLT, the same hierarchical classification of these medications was used.

**Determination of lipid levels**

LLT was evaluated on the index date to ensure that lipid measurements best reflected the impact of treatment. Relevant to the current analysis, at the time of the study, the ESC/EAS LDL-C treatment goal was <1.8 mmol/l (<70 mg/dl) or a ≥50% relative reduction for patients with ASCVD, DM type 2, and DM type 1 with target organ damage. For patients with DM not meeting the above criteria, LDL-C <2.5 mmol/l (<100 mg/dl) was the goal.[4] The guidelines also recommended non-HDL-C as a secondary target with treatment to goals of <2.6 mmol/l (<100 mg/dl) and <3.3 mmol/l (<130 mg/dl), respectively.[4]

The HAS recommended a therapeutic LDL-C goal of approximately <2.5 mmol/l (<100 mg/dl) for those with established cardiovascular disease and DM type 2 plus other risk factors.[5] Since administrative codes for DM do not allow for specificity of whether target organ damage was present, we analyzed achievement of both more and less stringent LDL-C and non-HDL-C goals for both ASCVD and DM.

## Cross-country comparison

LLT utilization and lipid goal achievement metrics from France were compared to data from a recent analysis which included a 2014 generalizable cohort with LLT prescriptions and lipid measurements from the UK General Practice Database.[10] In the UK cohort, Read codes (as opposed to French Thesaurus codes) defined the subgroups. For both countries, ASCVD subgroups were defined similarly. However, in the UK analysis, the DM subgroup selected had a somewhat higher risk based on the National Institute for Health and Care Excellence (NICE) 2014 guidelines.[10] As opposed to the French analysis, in the UK analysis, DM type 2 patients had to have a QRISK®2 10-year risk ≥10% and DM type 1 patients had to be age >40 years.[10] To permit cross-country comparisons, the same definition of statin intensity (used by NICE in 2014) was applied for both countries. Using this definition, atorvastatin 20 mg and rosuvastatin 10 mg were reclassified from the low-to-moderate category into a "high-dose" category. We used the term "dose," (e.g., high-dose statin) in this manuscript only when referring to cross-country comparisons. Statin dose categories for France and the UK (NICE 2014[11]) are summarized in Supplementary Table II.

## Statistical analysis

Statistical analyses were conducted with SAS® version 9.4 (SAS Institute, Inc, Cary, North Carolina) and were descriptive in nature. Demographics, clinical characteristics, LLT utilization, and achieved LDL-C and non-HDL-C levels were summarized via proportions and mean ± standard deviation, as appropriate. No formal statistical tests were performed to compare the LLT utilization and lipid goal achievement between the French data and the UK cohort.

## Results

The final study cohort included 32,924 patients (Supplementary Figure 2), of whom 51.5% had established ASCVD and the rest qualified due to the presence of DM. Mean age was 68.3 years, 58.9% were male, and 8.1% were smokers (Table I). Hierarchical classification yielded the following proportions in each category: recent ACS (0.9%); chronic CHD (31.0%); ischemic stroke/TIA (7.1%); PAD (12.6%); and DM (48.5%; Table I). Patient characteristics by prevalent categorizations are presented in Supplementary Table III.

The final study cohort was compared to another cohort from the same database, in which all patients met all inclusion criteria except presence of a valid LDL-C measurement in 2015. The characteristics of both cohorts were similar, suggesting that the results from the current analysis are generalizable to those without an LDL-C measurement (Supplementary Table IV). Comparison of baseline characteristics by statin treatment suggests that statin therapy was associated with higher utilization of other standard-of-care medications (Supplementary Table V).

### LLT utilization

Overall, only 47.5% of patients (55.8% of ASCVD and 38.7% of DM-only patients) were prescribed a statin as of the index date. Statins were overwhelmingly used as monotherapy (Table II and Figure 1A). In the overall cohort, 16.6% of those with ASCVD and 34.3% of those with DM had no evidence of any prior LLT treatment (Figure 1B).

Overall, 4.1% of ASCVD and 5.5% of DM-only patients were prescribed a regimen consisting only of non-statin LLT (eg, ezetimibe, fibrates, cholestyramine).

In these patients, ezetimibe was prescribed in 60.0% and 44.1% of the regimens for recent ACS and chronic CHD, respectively (Table II). When non-statin LLT was considered in addition to statins, only 52.3% of the total cohort (59.9% of ASCVD and 44.2% of DM) were prescribed any LLT as of the index date. LLT utilization by prevalent categorization is presented in Supplementary Table VI and Supplementary Figure 3.

***LDL-C and non-HDL-C goal achievement***

Among patients with ASCVD, only 13.9% achieved the LDL-C goal of <1.8 mmol/l. By hierarchical ASCVD categories, the LDL-C <1.8 mmol/l goal was achieved by 29.0% for recent ACS, 15.7% for chronic CHD, 12.3% for ischemic stroke/TIA, and 9.5% for PAD. In the DM-only group, LDL-C goal achievement was only 10.7% and 41.1% for LDL-C <1.8 mmol/l and <2.5 mmol/l, respectively (Supplementary Figure 4).

Non-HDL-C levels were available for 89.8% of patients who met the inclusion criteria for this study. The proportion of the ASCVD population achieving the non-HDL-C goal of <2.6 mmol/l was 25.6%. In the DM-only group, goal achievement was only 18.4% and 45.2% for non-HDL-C <2.6 mmol/l and <3.3 mmol/l, respectively (Supplementary Figure 5).

LDL-C and non-HDL-C goal achievement by prevalent classes is shown in Supplementary Figures 6 and 7, respectively; mean LDL-C and non-HDL-C are summarized in Supplementary Table VII.

***Comparison of results with a UK population (French data re-analyzed according to the UK statin categorization)***

Relative to the UK cohort,[10] the French cohort was prescribed statins less frequently. By categories, statins were prescribed to 87.1% versus 73.4% of patients with recent ACS, 81.9% versus 59.5% of chronic CHD, 73.2% versus 49.7% of ischemic stroke/TIA, 72.6% versus 49.0% of PAD, and 66.1% versus 38.8% of DM patients, in the UK versus France, respectively. High-dose statins were also prescribed more frequently in the UK (Table III). By categories, high-dose statins were prescribed to 62.4% versus 51.5% of patients with recent ACS, 34.6% versus 24.7% of patients with chronic CHD, 21.5% versus 18.3% of patients with ischemic stroke/TIA, 23.2% versus 11.0% of patients with PAD, and 17.0% versus 7.2% of the DM patients, for the UK versus French population respectively (Supplementary Table VIII). While treatment with only a non-statin LLT regimen was uncommon in both countries, ezetimibe was used in these regimens more frequently in the UK: 61.6% versus 36.9% of patients in the ASCVD cohorts and 63.4% versus 14.5% of the DM patients, respectively.

Overall, compared with the 2014 UK population,[10] LDL-C and non-HDL-C goal achievement were less frequent in the 2015 French population (Table IV). This overall disparity carried through to the disease categories. By hierarchical categories of ASCVD patients, LDL-C <1.8 mmol/l was achieved in the UK versus French patients in 43.8% versus 29.0% for those with recent ACS, 32.0% versus 15.7% for those with chronic CHD, 28.4% versus 12.3% for those with ischemic stroke/TIA, and 26.4% versus 9.5% for those with PAD. For DM patients, LDL-C <1.8 mmol/l was achieved in UK and French cohorts in 26.0% versus 10.7%, respectively. By hierarchical categories of ASCVD patients, non-HDL-C <2.6 mmol/l was achieved in

the UK patients versus French patients in 54.5% versus 41.6% for those with recent ACS, 43.0% versus 28.4% for those with chronic CHD, 41.5% versus 25.0% for those with ischemic stroke/TIA, and 36.9% versus 18.0% for those with PAD. For DM patients, non-HDL-C <2.6 mmol/l was achieved in 33.2% of UK and 16.3% of French cohorts.

## Discussion

This study provides evidence from 2015 on LLT utilization and guideline-recommended lipid goal achievement in a generalizable French population using point-in-time assessment of LLT prescriptions and lipid measurements. It also provides data on LLT usage and lipid goal achievement for understudied populations in France, including those with ischemic stroke/TIA and PAD.

In this study, only 55.8% of patients with ASCVD and 38.7% with DM were currently prescribed a statin. Of those patients without a current LLT prescription, 41.4% with ASCVD and 61.6% with DM had no evidence of an LLT prescription within the previous 2 years. These findings highlight a significant gap between clinical practice and existing practice guidelines.[4] In comparison to the 2006–2007 MONA LISA study,[8] our findings demonstrate that statin utilization remains inadequate, contributing to a LDL-C <1.8 mmol/l achievement by only 13.9% of patients with ASCVD and 10.7% with DM without ASCVD.

Prior studies, many of which are less generalizable (based on database or study selection characteristics), have reported higher medication utilization than the current study. For example, 77.6% of all patients with coronary artery disease (CAD) in the French cohort of the REACH registry were treated with statins.[12] Studies from highly selected cohorts have reported even higher statin utilization, such as 92.2% for a similar population in the CORONOR study.[12, 13] In contrast, we found that 59.9% of all patients with recent ACS and/or chronic CHD were prescribed statins, a finding that our analysis suggests is generalizable to similar populations across France.

With regard to treatment of prior ischemic stroke/TIA, a French study from 2006–2010 reported only 20.1% statin utilization in such patients but with no evidence of

CAD or PAD.[14] The French cohort of the REACH registry has reported statin utilization of 58.0% in patients with cerebrovascular disease (including ischemic stroke/TIA) with or without CHD and/or PAD.[12] In comparison, for those with prior ischemic stroke/TIA, we found 49.6% statin use among patients without evidence of CAD and 52.1% use in any patient with prior stroke or TIA.

With regard to treatment of PAD, two French studies, one conducted in 2003[15] and the other from 2006–2010,[14] reported 53% and 33.8% statin utilization, respectively, in patients with PAD but without CAD, stroke, or TIA. The REACH registry found that 62.7% of all their PAD patients received statins.[12] Investigators in the ATTEST study found a statin prescription rate of 53% among patients with PAD alone compared with 71% for PAD with CAD or cerebrovascular disease, and 74% for CAD and/or cerebrovascular disease without PAD.[15] In comparison, we found 48.9% statin use in PAD patients without CAD, stroke, or TIA, and 54.2% use in any patient with PAD.

With regard to treatment of DM without ASCVD, according to patient samples from the 2007 ENTRED[16] and 2008 DIABASIS national surveys,[17] statins were prescribed to 47% of French patients with type 2 DM, an appreciable increase from the 25% identified in a 2001 ENTRED sample.[16, 17] Although the ENTRED data are generalizable, patients and providers had to agree to participate, making the data less generalizable compared with the present study. In comparison, we found 38.7% statin utilization in patients with DM types 1 and 2 but without ASCVD. Since DM type 1 was not included as an indication for statin treatment in the HAS guidelines, it is likely that this group was less well-treated than those with DM type 2.

Comparison of the French population with a similar UK population analyzed by a similar hierarchical classification methodology highlighted a substantially lower overall statin and high-dose statin use as well as lower LDL-C goal achievement in France. A recent study conducted in the Netherlands using the same methodology demonstrated similar findings with higher statin utilization rate and LDL-C goal achievement when compared with the present French population.[18] It is worth noting that the Dutch analysis only included ischemic stroke, unlike the French analysis which included TIA along with ischemic stroke.

Furthermore, data from the observational Dyslipidemia International Study (DYSIS) registry are also consistent with our findings; the mean atorvastatin (or equivalent) dose in the French cohort ranged from 20 mg/day between 2008–2012 to 30 mg/day between 2013–2014, suggesting that many patients received low-to-moderate intensity therapy.[19] In DYSIS, only 20.6% of French patients overall reached their LDL-C targets, compared with 40.9% in the UK; seven other European countries had similar or lower rates of goal achievement than France.[20]

Surveys combining data from multiple European countries have reported varying use of LLTs and achievement of guidance-recommended lipid goal achievement. For example, in the EUROASPIRE III (2006–2007) survey of 8917 patients with CHD from 22 European countries, 79.8% (range 41.6%–95.4%) were reported to have been treated with LLTs, and only 45.5% (3561/6529) achieved LDL-C levels <2.5 mmol/L.[21] In this survey, 89.1% were reported to have used statins in France and 61.7% (195/316) achieved LDL-C levels <2.5 mmol/L.[21] In the EUROASPIRE IV (2014–2015) survey analysis of 4579 patients at high risk of cardiovascular disease, 35.6% were on LLTs, of whom 96.1% were on statins.[22] Only 32.7% of those

prescribed LLTs achieved LDL-C <2.5 mmol/L.[22] Of the 1158 and 2183 patients with newly diagnosed and previously known diabetes, respectively, from the EUROASPIRE IV survey, more than 80% were prescribed statins, with 18% and 28% achieving LDL-C levels <1.8 mmol/L, and 56% and 66% achieving LDL-C levels <2.5 mmol/L, respectively.[23] However, because of the difference in patient selection procedure, population size, and study design, compared with our study, it is not possible to compare the results from the surveys with our findings.

The established challenge of patient adherence to statins has been demonstrated in a French population study.[24] More recent challenges to appropriate usage of statins in France arose with the publication that called into question the validity of the “cholesterol hypothesis” and the evidence demonstrating the benefits of statins in preventing cardiovascular events.[25] Despite rapid response by a consortium of medical and patient associations,[26] the publication was associated with an increased probability of statin discontinuation compared to a historical reference period by about 25% in high-risk (secondary prevention) and 40% in moderate-risk (diabetic) patients; this increase in statin discontinuation was associated with a greater risk of all-cause mortality.[26] Complaints of muscle-related adverse effects increased dramatically. Although statin-associated muscle symptoms are a principal cause of statin non-adherence and/or discontinuation, myopathy is observed in only 0.1%–0.01% of patients taking a statin.[27] This is also supported by a systematic review which reported muscle symptoms as the most important adverse effect of statin treatment but re-emphasized the very low incidence of myopathy in randomized placebo-controlled clinical trials of statins.[28] A 2002 joint Agence Française de Sécurité Sanitaire des Produits de Santé-European Medicines Agency

study affirmed that no general musculoskeletal contraindication to statin use is warranted.[29]

Government regulations may also play a role in suboptimal LLT utilization. In 2014, the French Ministry of Social Affairs and Health implemented a requirement for submission of forms requesting prescription of rosuvastatin or ezetimibe.[30] In addition, neither atorvastatin nor rosuvastatin are indicated by the HAS guidelines for secondary prevention.[5, 6]

Beyond provider and public education on the benefits and safety of statins, performance improvement initiatives are needed to increase prescription and adherence rates. For those patients who are adherent to statins and still do not achieve lipid goals, or for those who are truly intolerant of statins even after multiple rechallenges, expanding the use of validated non-statin LLT should be considered. Ezetimibe, and the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors evolocumab and alirocumab, have been shown in the IMPROVE-IT, FOURIER, and ODYSSEY OUTCOMES studies, respectively, to reduce cardiovascular events on top of statin therapy.[31-33]

Analysis of medication adherence in the form of filled prescriptions typically has limitations in large, generalizable populations. Written prescription data overestimate patient medication adherence, as many do not fill their prescriptions or take their prescriptions as recommended. Thus, our analysis likely reflects an optimistic assessment of true medication adherence in the form of filled prescriptions in France. In addition, while our analysis suggests that patients with and without a LDL-C measurement were similar, these measurements were collected during clinical practice and thus were not prospectively specified. Lastly, our study was not

designed to explore the causes for the observed sub-optimal use of statins in the French population compared with other European countries such as the UK.

In conclusion, this study demonstrates suboptimal statin utilization among patients with established ASCVD and/or DM in a generalizable 2015 French population. Achievement of LDL-C and non-HDL-C goals as recommended by the 2011 ESC/EAS guidelines were also suboptimal. The analysis also provides novel evidence about the treatment of previously understudied subgroups of high-risk patients. The gap between existing treatment and the guideline recommendations can best be decreased through a multicomponent strategy.

## Conflict of interest statement

JF has received grants and speaker's fees from Amgen, Merck, and Sanofi, and speaker's fees from AstraZeneca. KG was an employee of Sanofi at the time of this study. SRI is an employee of Regeneron Pharmaceuticals, Inc. DA was an employee of IQVIA at the time of this study. DLS has received modest consultant/advisory fees from Sanofi and Regeneron Pharmaceuticals, Inc.

## Acknowledgements

This work was supported by Sanofi and Regeneron Pharmaceuticals, Inc.

Medical writing support under the direction of the authors was provided by Emmanuel Ogunnowo, PhD, of Prime (Knutsford, UK) and Jeff Alexander of SNELL Medical Communication Inc. (Quebec, Canada), supported by Sanofi and Regeneron Pharmaceuticals, Inc., according to Good Publication Practice guidelines (Link). The sponsors were involved in the study design and collection, analysis, and interpretation of data, as well as data checking of information provided in the manuscript. The authors were responsible for all content and editorial decisions and received no honoraria related to the development of this publication.

JF was involved with the design of the study, interpretation of data and critical review of drafts. KG was involved with the design of the study, interpretation of data, and critical review of drafts. SRI was involved with the design of the study, interpretation of data, and critical review of drafts. DA was involved with the design of the study, acquisition, analysis and interpretation of data, and critical review of drafts. DLS was involved with the design of the study, interpretation of data, and critical review of drafts. All authors provided final approval of the submitted manuscript.

## References


**1.** World Health Organization. Noncommunicable diseases country profiles 2014: France. 2014. Available at: http://www.who.int/nmh/countries/fra_en.pdf.

**2.** Wilkins E, Wilson L, Wickramasinghe K, et al. European cardiovascular disease statistics 2017. Available at: http://www.ehnheart.org/cvd-statistics.html

**3.** Danchin N, Puymirat E, Aissaoui N, Adavane S, Durand E. [Epidemiology of acute coronary syndromes in France and in Europe]. *Ann Cardiol Angeiol (Paris).* 2010;59 Suppl 2:S37-41.

**4.** Reiner Z, Catapano AL, De Backer G, et al. ESC/EAS Guidelines for the management of dyslipidaemias: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J.* 2011;32:1769-1818.

**5.** Haute Autorité de Santé. Bon usage des médicaments: Prévention cardio-vasculaire: le choix de la statine la mieux adaptée dépend de son efficacité et de son efficience. 2012. Available at: https://www.has-sante.fr/portail/upload/docs/application/pdf/2012-02/statine_-_fiche_bum.pdf.

**6.** Haute Autorité de Santé. Main dyslipidaemias: Management strategies. 2017. Available at: https://www.has-sante.fr/portail/upload/docs/application/pdf/2017-09/synthes_fiche_memo_dyslipidemies_1.pdf.

**7.** Ferrieres J, Bongard V, Dallongeville J, et al. Trends in plasma lipids, lipoproteins and dyslipidaemias in French adults, 1996-2007. *Arch Cardiovasc Dis.* 2009;102:293-301.

**8.** Bongard V, Dallongeville J, Arveiler D, et al. Attainment of low-density lipoprotein cholesterol target in the French general population according to levels of cardiovascular risk: Insights from the MONA LISA study. *Arch Cardiovasc Dis.* 2013;106:93-102.

**9.** Jouaville SL, Miotti H, Coffin G, Sarfati B, Meilhoc A. Validity and limitations of the Longitudinal Patient Database France for use in pharmacoepidemiological and pharmacoeconomics studies. *Value Health.* 2015;18:A18.

**10.** Steen DL, Khan I, Ansell D, Sanchez RJ, Ray KK. Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK in 2014: Comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. *BMJ Open.* 2017;7:e013255.

**11.** National Institute for Health and Care Excellence. Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Clinical guideline CG181. 2014. Available at: http://www.nice.org.uk/guidance/cg181.

**12.** Smolderen KG, Wang K, de Pouvourville G, et al. Two-year vascular hospitalisation rates and associated costs in patients at risk of atherothrombosis in France and Germany: Highest burden for peripheral arterial disease. *Eur J Vasc Endovasc Surg.* 2012;43:198-207.

**13.** Meurice T, Tricot O, Lemesle G, et al. Prevalence and correlates of non-optimal secondary medical prevention in patients with stable coronary artery disease. *Arch Cardiovasc Dis.* 2015;108:340-346.

**14.** Bejot Y, Zeller M, Lorgis L, et al. Secondary prevention in patients with vascular disease. A population based study on the underuse of recommended medications. *J Neurol Neurosurg Psychiatry.* 2013;84:348-353.

**15.** Blacher J, Cacoub P, Luizy F, et al. Peripheral arterial disease versus other localizations of vascular disease: The ATTEST study. *J Vasc Surg.* 2006;44:314-318.

**16.** Jaffiol C. [Current management of type 2 diabetes in France]. *Bull Acad Natl Med.* 2009;193:1645-1661.

**17.** Marant C, Romon I, Fosse S, et al. French medical practice in type 2 diabetes: The need for better control of cardiovascular risk factors. *Diabetes Metab.* 2008;34:38-45.

**18.** Kuiper JG, Sanchez RJ, Houben E, et al. Use of lipid-modifying therapy and LDL-C goal attainment in a high-cardiovascular-risk population in the Netherlands. *Clin Ther.* 2017;39:819-827.e811.

**19.** Ferrieres J, Rouyer MV, Lautsch D, et al. Improvement in achievement of lipid targets in France: Comparison of data from coronary patients in the DYSIS and DYSIS II studies. *Int J Cardiol.* 2016;222:793-794.

**20.** Gitt AK, Lautsch D, Ferrieres J, et al. Contemporary data on low-density lipoprotein cholesterol target value attainment and distance to target in a

cohort of 57,885 statin-treated patients by country and region across the world. *Data Brief.* 2016;9:616-620.

**21.** Reiner Z, De Bacquer D, Kotseva K, et al. Treatment potential for dyslipidaemia management in patients with coronary heart disease across Europe: findings from the EUROASPIRE III survey. *Atherosclerosis.* 2013;231:300-307.

**22.** Kotseva K, De Bacquer D, De Backer G, et al. Lifestyle and risk factor management in people at high risk of cardiovascular disease. A report from the European Society of Cardiology European Action on Secondary and Primary Prevention by Intervention to Reduce Events (EUROASPIRE) IV cross-sectional survey in 14 European regions. *Eur J Prev Cardiol.* 2016;23:2007-2018.

**23.** Gyberg V, De Bacquer D, De Backer G, et al. Patients with coronary artery disease and diabetes need improved management: a report from the EUROASPIRE IV survey: a registry from the EuroObservational Research Programme of the European Society of Cardiology. *Cardiovasc Diabetol.* 2015;14:133.

**24.** Latry P, Molimard M, Dedieu B, Couffinhal T, Begaud B, Martin-Latry K. Adherence with statins in a real-life setting is better when associated cardiovascular risk factors increase: A cohort study. *BMC Cardiovasc Disord.* 2011;11:46.

**25.** Even P. *Corruptions et crédulité en médecine: Stop aux statines et autres dangers*. Paris: Cherche Midi; 2015.

**26.** Bezin J, Francis F, Nguyen NV, et al. Impact of a public media event on the use of statins in the French population. *Arch Cardiovasc Dis.* 2017;110:91-98.

**27.** Stroes ES, Thompson PD, Corsini A, et al. Statin-associated muscle symptoms: Impact on statin therapy-European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. *Eur Heart J.* 2015;36:1012-1022.

**28.** Simic I, Reiner Z. Adverse effects of statins - myths and reality. *Curr Pharm Des.* 2015;21:1220-1226.

**29.** AGENCE FRANCAISE DE SECURITE SANITAIRE DES PRODUITS DE SANTE. Mise au point sur les risques musculaires des statines. 2002. Available at: http://ansm.sante.fr/var/ansm_site/storage/original/application/c6090fc66b0777de27e12faf285d4be4.pdf.

**30.** Ministère des Affaires Sociales de la Santé et des Droits des Femmes. Décision du 24 juin 2014 relative à la procédure d'accord préalable pour bénéficier de la prise en charge des médicaments hypocholestérolémiants suivants: L'ézétimibe, qu'il soit pris seul ou en association fixe avec de la simvastatine. 2014. Available at: https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000029490152.

**31.** Cannon CP, Giugliano RP, Blazing MA, et al. Rationale and design of IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial): comparison of ezetimbe/simvastatin versus simvastatin

monotherapy on cardiovascular outcomes in patients with acute coronary syndromes. *Am Heart J.* 2008;156:826-832.

**32.** Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med.* 2017;376:1713-1722.

**33.** Steg P. Cardiovascular outcomes with alirocumab after acute coronary syndrome: results of the ODYSSEY outcomes trial. *Presented at the 67th Annual Scientific Session of the American College of Cardiology (ACC), 10-12 March 2018 (Presentation number 401-08).* Orlando, FL, USA.

**Table I. Patient characteristics for the overall study cohort and hierarchical disease categories.**

| | Total cohort N = 32,924 | Recent ACS n = 293 | Chronic CHD n = 10,213 | Ischemic stroke/TIA n = 2324 | PAD n = 4132 | DM n = 15,962 |
|---|---|---|---|---|---|---|
| **Demographics** | | | | | | |
| Age, mean (SD) | 68.3 (12.2) | 64.2 (14.1) | 71.0 (11.7) | 69.7 (13.0) | 71.0 (11.4) | 65.8 (11.9) |
| Male, % | 58.9 | 73.7 | 69.4 | 52.3 | 62.3 | 52.0 |
| **Cardiovascular risk conditions, %** | | | | | | |
| Recent ACS | 0.9 | 100 | N/A | N/A | N/A | N/A |
| Chronic CHD | 31.8 | 87.4 | 100 | N/A | N/A | N/A |
| Ischemic stroke/TIA | 8.4 | 3.8 | 4.2 | 100 | N/A | N/A |
| PAD | 18.4 | 10.2 | 16.2 | 10.8 | 100 | N/A |
| DM | 63.9 | 17.7 | 32.0 | 23.9 | 29.2 | 100 |
| **Behaviors and comorbidities of interest, %** | | | | | | |
| Current smokers | 8.1 | 14.3 | 8.4 | 6.9 | 14.1 | 6.4 |
| Hypertension | 67.6 | 45.1 | 64.3 | 67.3 | 72.0 | 69.2 |
| History of CHF[a] | 3.6 | 2.7 | 6.8 | 2.4 | 2.8 | 2.0 |
| CKD | 1.9 | 1.4 | 2.4 | 2.2 | 2.8 | 1.3 |
| Stage V[b] | 0.2 | 0 | 0.2 | 0.1 | 0.2 | 0.1 |
| Dementia[a] | 0.5 | 0.3 | 0.5 | 1.1 | 0.5 | 0.4 |
| COPD[a] | 10.1 | 9.6 | 12.8 | 8.4 | 16.9 | 6.9 |
| Diagnosis associated with musculoskeletal pain | 87.4 | 86.7 | 88.9 | 86.4 | 89.6 | 86.0 |
| Moderate/severe liver disease[a] | 0.3 | 0 | 0.1 | 0.1 | 0.3 | 0.4 |
| **Concomitant medications, %** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Beta-blockers | 44.9 | 77.8 | 71.1 | 34.3 | 31.9 | 32.3 |
| ACEIs/ARBs | 65.8 | 74.4 | 72.8 | 64.7 | 63.5 | 61.9 |
| Clopidogrel | 19.3 | 20.8 | 38.3 | 21.3 | 33.1 | 3.3 |

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; N/A = not applicable; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

[a]Based on Quan-Charlson comorbidity scale components.

[b]Stage V includes end-stage renal disease and dialysis.

**Table II. LLT use in the overall study cohort and hierarchical disease categories.**

| % | Total cohort N = 32,924 | Recent ACS n = 293 | Chronic CHD n = 10,213 | Ischemic stroke/TIA n = 2324 | PAD n = 4132 | DM n = 15,962 |
|---|---|---|---|---|---|---|
| High-intensity statin | 6.9 | 43.3 | 13.3 | 10.4 | 4.5 | 2.3 |
| Monotherapy | 92.2 | 98.4 | 91.0 | 95.0 | 92.4 | 92.4 |
| Plus ezetimibe | 7.4 | 1.6 | 8.7 | 5.0 | 6.5 | 6.8 |
| Plus fibrate | 0.3 | 0 | 0.2 | 0 | 0.5 | 0.5 |
| Plus other non-statin LLT | 0.1 | 0 | 0.1 | 0 | 0.5 | 0.3 |
| Low-to-moderate-intensity statin | 40.6 | 30.0 | 46.2 | 39.2 | 44.4 | 36.4 |
| Monotherapy | 89.3 | 95.5 | 84.4 | 93.3 | 91.5 | 91.7 |
| Plus ezetimibe | 10.1 | 4.5 | 15.0 | 6.4 | 7.8 | 7.4 |
| Plus fibrate | 0.1 | 0 | 0.1 | 0.2 | 0.1 | 0.2 |
| Plus other non-statin LLT | 0.6 | 0 | 0.5 | 0.1 | 0.6 | 0.7 |
| Non-statin LLT only | 4.8 | 1.7 | 3.8 | 3.7 | 5.1 | 5.5 |
| Ezetimibe | 24.4 | 60.0 | 44.1 | 22.4 | 28.9 | 14.5 |
| Fibrate | 74.6 | 40.0 | 53.8 | 75.3 | 70.1 | 85.1 |
| Other non-statin LLT | 1.0 | 0 | 2.0 | 2.4 | 0.9 | 0.5 |
| Evidence of prior LLT | 22.5 | 14.7 | 23.9 | 22.5 | 23.6 | 21.4 |
| High-intensity statin | 29.0 | 58.1 | 42.8 | 35.6 | 26.1 | 20.9 |
| Low-to-moderate-intensity statin | 57.9 | 41.9 | 50.8 | 56.2 | 65.6 | 65.9 |
| Non-statin LLT | 9.5 | 0 | 6.4 | 8.2 | 8.3 | 13.2 |
| No evidence of prior LLT | 25.2 | 10.2 | 12.7 | 24.2 | 22.4 | 34.3 |

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Numbers in the gray bars denote absolute percentages. They add up to 100% when added vertically for each column. Numbers in the white bars are relative percentages of the absolute percentages in the gray bars. Subcategories in the white bars are hierarchical. ASCVD subgroups represent hierarchical categorization.

**Table III. Comparison of LLT utilization between the UK[10] and French study populations.**

| % | ASCVD | | DM | |
|---|---|---|---|---|
| | **UK (n = 91,479)** | **France (n = 16,962)** | **UK[a] (n = 56,962)** | **France (n = 15,962)** |
| **High-dose statin** | 31.4 | 20.9 | 18.7 | 7.2 |
| Monotherapy | 92.2 | 93.9 | 92.0 | 95.9 |
| Plus ezetimibe | 4.1 | 5.9 | 2.6 | 3.4 |
| **Moderate-dose statin** | 42.1 | 23.9 | 42.6 | 20.6 |
| Monotherapy | 98.2 | 80.1 | 98.2 | 86.7 |
| Plus ezetimibe | 1.0 | 19.0 | 0.8 | 12.0 |
| **Low-dose statin** | 5.6 | 11.0 | 4.8 | 11.0 |
| Monotherapy | 96.3 | 95.6 | 96.1 | 98.6 |
| Plus ezetimibe | 2.8 | 4.2 | 0.9 | 1.2 |
| **Non-statin only** | 1.9 | 4.1 | 1.7 | 5.5 |
| Ezetimibe | 61.6 | 36.9 | 63.4 | 14.5 |
| **No evidence of prior LLT** | 6.5 | 16.6 | 22.1 | 34.3 |

ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; LLT = lipid-lowering therapy.

Data are percentages. French data re-analyzed according to the UK statin dose definition.

[a]UK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population.

**Table IV. Achievement of LDL-C and non-HDL-C goals – comparison between French and UK[10] populations.**

| % | ASCVD | | DM | |
|---|---|---|---|---|
| | UK (n = 91,479) | France (n = 16,962) | UK[a] (n=56,962) | France (n=15,962) |
| **LDL-C <1.8 mmol/l** | | | | |
| High-dose statin | 37.3 | 22.2 | 36.8 | 20.3 |
| Moderate-dose statin | 37.8 | 19.1 | 41.0 | 19.9 |
| Low-dose statin | 22.9 | 8.9 | 26.4 | 9.4 |
| Non-statin LLT | 6.4 | 5.3 | 6.1 | 4.5 |
| **LDL-C <2.5 mmol/l** | | | | |
| High-dose statin | 78.9 | 70.9 | 74.2 | 61.2 |
| Moderate-dose statin | 81.9 | 65.7 | 79.0 | 63.6 |
| Low-dose statin | 68.3 | 44.3 | 65.7 | 44.4 |
| Non-statin LLT | 32.3 | 27.6 | 31.0 | 29.0 |
| **Non-HDL-C <2.6 mmol/l**[b] | | | | |
| High-dose statin | 47.9 | 42.9 | 41.5 | 29.2 |
| Moderate-dose statin | 52.1 | 37.7 | 49.4 | 33.6 |
| Low-dose statin | 36.8 | 19.4 | 35.8 | 16.8 |
| Non-statin LLT | 12.1 | 10.0 | 9.5 | 9.1 |
| **Non-HDL-C <3.3 mmol/l**[b] | | | | |
| High-dose statin | 79.5 | 74.5 | 72.3 | 62.3 |
| Moderate-dose statin | 84.4 | 71.5 | 79.3 | 66.2 |
| Low-dose statin | 73.7 | 53.2 | 66.8 | 47.5 |
| Non-statin LLT | 40.0 | 35.5 | 35.1 | 33.0 |

ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy; non-HDL-C = non-high-density lipoprotein cholesterol.

French data re-analyzed according to the UK statin dose definition.

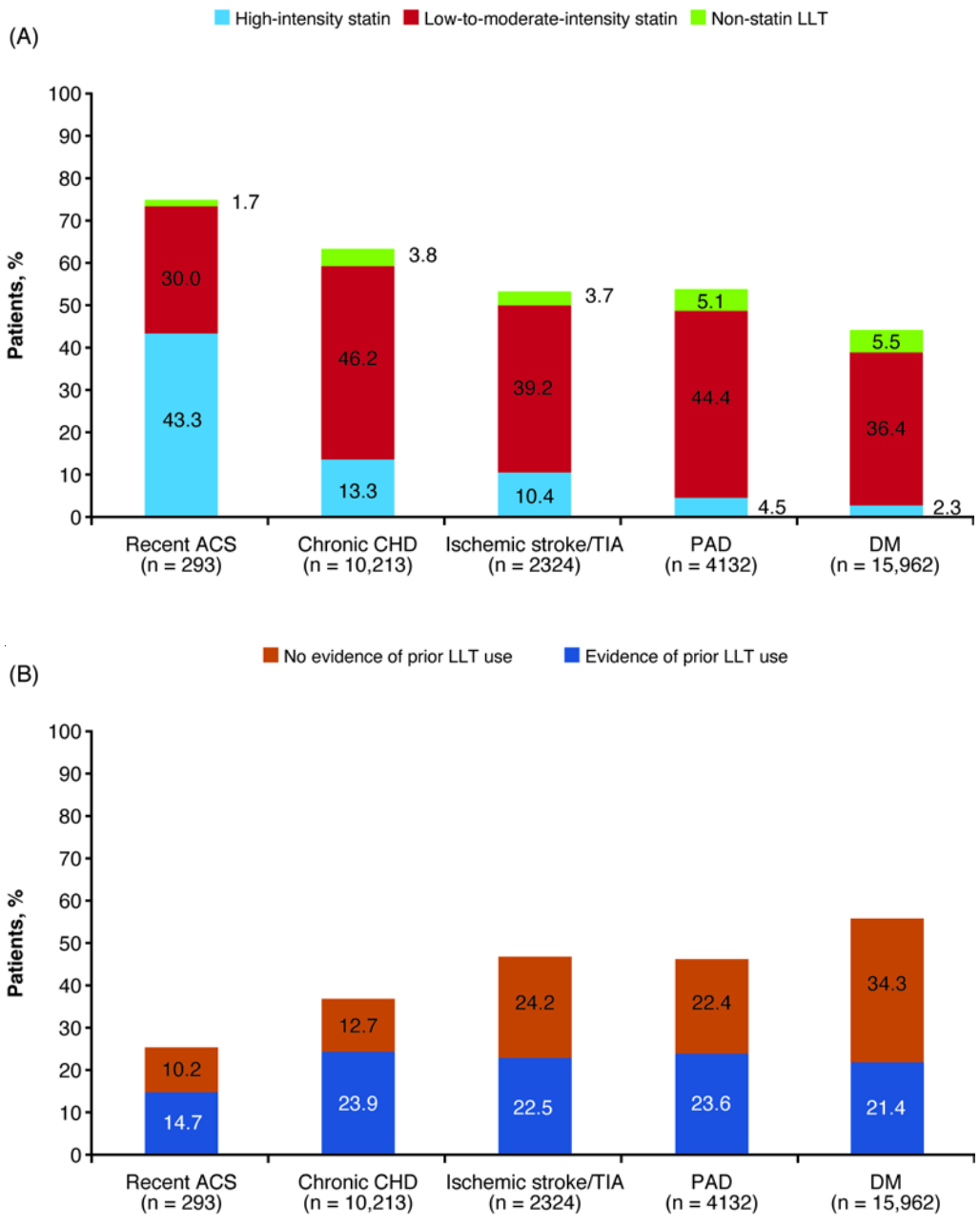
[a]UK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population.

[b]Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data.

## Figure captions

**Figure 1. Absolute proportions of LLT treatment by hierarchical disease categories in (A) treated and (B) non-treated patients.** ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

**Figure 1.**


(A)
High-intensity statin
Low-to-moderate-intensity statin
Non-statin LLT
Patients, %
100
90
80
70
60
50
40
30
20
10
0
43.3
30.0
1.7
13.3
46.2
3.8
10.4
39.2
3.7
4.5
44.4
5.1
2.3
36.4
5.5
Recent ACS (n = 293)
Chronic CHD (n = 10,213)
Ischemic stroke/TIA (n = 2324)
PAD (n = 4132)
DM (n = 15,962)
(B)
No evidence of prior LLT use
Evidence of prior LLT use
Patients, %
14.7
10.2
23.9
12.7
22.5
24.2
23.6
22.4
21.4
34.3
Recent ACS (n = 293)
Chronic CHD (n = 10,213)
Ischemic stroke/TIA (n = 2324)
PAD (n = 4132)
DM (n = 15,962)

# Supplementary Material

## Supplementary Table I. French Thesaurus codes for disease categorization.

| Cardiovascular risk level | Disease category | Brief code description | Code | Description |
|---|---|---|---|---|
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128101 | Recurrent MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128092 | MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128095 | Complicated MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128683 | Q-wave MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128685 | Non-Q-wave MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128748 | Q-wave MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128750 | Non-Q-wave MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128883 | Anterior MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128884 | Inferior MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 128885 | Lateral MI |
| 01 - Recent ACS<br>02 - CHD | 01 - MI | Acute MI | 143638 | MI |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 128077 | New-onset angina pectoris |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 128080 | Unstable angina pectoris |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 128083 | Vasospastic angina pectoris |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 128110 | UNSTABLE ANGINA PECTORIS (ANGINA STATUS) **DELETED** |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 143723 | Angina decubitus |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 143724 | Unstable angina pectoris |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 128110 | UNSTABLE ANGINA PECTORIS (ANGINA STATUS) **DELETED** |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 144977 | Overlapping angina attacks |
| 01 - Recent ACS<br>02 - CHD | 02 - Angina | Unstable angina | 144979 | Syncopal angina pain |

| | | | | |
|---|---|---|---|---|
| 01 - Recent ACS 02 - CHD | 02 - Angina | Unstable angina | 128784 | Angina at rest |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 277193 | ACS |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 128878 | ACS |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 128879 | ACS with elevated enzyme levels |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 128880 | ACS with normal enzyme levels |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 128156 | Dressler syndrome |
| 01 - Recent ACS 02 - CHD | 03 - Other ACS | Other ACS | 128153 | Acute pericarditis of MI |
| 02 - CHD | 02 - Angina | Stable angina | 219794 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 264549 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 143722 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 128065 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 128068 | Spontaneous angina |
| 02 - CHD | 02 - Angina | Stable angina | 128071 | Complicated angina of multiple origin |
| 02 - CHD | 02 - Angina | Stable angina | 128074 | Stable angina |
| 02 - CHD | 02 - Angina | Stable angina | 128459 | Angina with normal coronary arteries |
| 02 - CHD | 02 - Angina | Stable angina | 128597 | Prinzmetal angina |
| 02 - CHD | 02 - Angina | Stable angina | 128838 | Angina |
| 02 - CHD | 02 - Angina | Stable angina | 143151 | Abdominal angina |
| 02 - CHD | 02 - Angina | Stable angina | 143632 | ANGINA, CORONARY INSUFFICIENCY **DELETED |
| 02 - CHD | 02 - Angina | Stable angina | 143677 | Angina |
| 02 - CHD | 02 - Angina | Stable angina | 128459 | Angina with normal coronary arteries |
| 02 - CHD | 02 - Angina | Stable angina | 128653 | Coronary insufficiency |
| 02 - CHD | 02 - Angina | Stable angina | 128673 | Syndrome X (coronary insufficiency) |
| 02 - CHD | 02 - Angina | Stable angina | 150652 | Angina pain |
| 02 - CHD | 02 - Angina | Stable angina | 151262 | Angina pain |
| 02 - CHD | 02 - Angina | Stable angina | 143632 | ANGINA, CORONARY INSUFFICIENCY **DELETED** |
| 02 - CHD | 02 - Angina | Stable angina | 184202 | Angina pain |
| 02 - CHD | 02 - Angina | Stable angina | 275961 | Angina pectoris |
| 02 - CHD | 02 - Angina | Stable angina | 139971 | Angina pain |

| | | | | |
|---|---|---|---|---|
| 02 - CHD | 02 - Angina | Stable angina | 144858 | Angina pain |
| 02 - CHD | 02 - Angina | Stable angina | 143725 | Prinzmetal angina |
| 02 - CHD | 02 - Angina | Stable angina | 150607 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 204160 | Effort angina |
| 02 - CHD | 02 - Angina | Stable angina | 277164 | Coronary spasm |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128089 | Coronary atherosclerosis |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 277168 | Three-vessel coronary stenosis |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 180366 | Coronary insufficiency |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 270115 | Stenosis of a coronary artery |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 275982 | Three-vessel coronary disease |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143678 | Coronary insufficiency |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128762 | CHD |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128881 | CHD |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 270052 | Coronary artery dilatation with active stent |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128578 | Coronary artery dilatation without stent |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128581 | Coronary artery dilatation with stent |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143434 | Coronary artery dilatation without stent |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143435 | Coronary artery dilatation with stent |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128575 | Post-MI repair of ventricular ectasia |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143684 | Chronic ischemic heart disease |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128107 | Silent ischemia |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128496 | Mitral insufficiency due to ischemic heart disease |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128679 | Chronic ischemic heart disease |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128730 | Ischemic mitral insufficiency |

| | | | | |
|---|---|---|---|---|
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128768 | Ischemic cardiomyopathy |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128098 | Sequelae of MI |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 179983 | Cardiac monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128462 | Post-MI monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128104 | Cardiac readaptation |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143631 | Coronary angioplasty |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 277190 | Post-coronary angioplasty monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 277178 | Coronary disease follow-up |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128371 | Coronary bypass |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 128465 | Coronary artery bypass grafting monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 143646 | Coronary bypass |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 151044 | Coronary artery bypass grafting monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 263433 | Coronary artery bypass grafting monitoring |
| 02 - CHD | 06 - CHD Diagnosis | Other chronic ischemic heart disease | 270166 | Coronary artery bypass grafting monitoring |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133505 | Cerebral ischemic accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140329 | Cerebral ischemic accident due to another etiology |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140330 | Cerebral ischemic accident of undetermined etiology |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 143292 | Cerebral ischemic accident of the anterior cerebral artery |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 143293 | Cerebral ischemic accident of the posterior cerebral artery |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 128170 | Progressive carotid vascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 128173 | Carotid vascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134444 | Cerebral infarction due to thrombosis of the precerebral arteries |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134446 | Cerebral infarction due to embolism of the precerebral arteries |

| | | | | |
|---|---|---|---|---|
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134448 | Cerebral infarction due to occlusion or stenosis of the precerebral arteries |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 144224 | Ischemic cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133512 | Recurrent cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133516 | Arteriopathic cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133522 | Vascular accident affecting the middle cerebral artery |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133524 | Vascular accident affecting the anterior cerebral artery |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134450 | Cerebral infarction due to thrombosis of the cerebral arteries |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134452 | Cerebral infarction due to embolism of the cerebral arteries |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134454 | Cerebral infarction due to occlusion or stenosis of the cerebral arteries |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140320 | Cerebral ischemic accident of the sylvian fissure |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140321 | Cerebral ischemic accident of the superficial artery of the sylvian fissure |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140322 | Cerebral ischemic accident of the deep artery of the sylvian fissure |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140324 | Cerebral ischemic accident due to cardiac embolism |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140325 | Cerebral ischemic accident due to arterial embolism |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140327 | Cerebral ischemic accident due to stenosis, atherothrombosis |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 140327 | Cerebral ischemic accident due to stenosis, atherothrombosis |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133501 | Cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 133503 | Evolving cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 144150 | Cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 208582 | Cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 276482 | Cerebrovascular accident |
| 03 - Ischemic stroke | 04 - Stroke | Ischemic stroke | 134460 | Cerebral infarction |
| 04 - PAD | 05 - PAD | PVD | 134470 | Occlusion and stenosis of precerebral arteries, multiple and bilateral |
| 04 - PAD | 05 - PAD | PVD | 134472 | Occlusion and stenosis of another precerebral artery |

| | | | | |
|---|---|---|---|---|
| 04 - PAD | 05 - PAD | PVD | 134474 | Occlusion and stenosis of a precerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134476 | Occlusion and stenosis of the middle cerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134478 | Occlusion and stenosis of the anterior cerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134480 | Occlusion and stenosis of the posterior cerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134482 | Occlusion and stenosis of cerebellar arteries |
| 04 - PAD | 05 - PAD | PVD | 134484 | Occlusion and stenosis of cerebral arteries, multiple and bilateral |
| 04 - PAD | 05 - PAD | PVD | 134486 | Occlusion and stenosis of another cerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134488 | Occlusion and stenosis of a cerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134470 | Occlusion and stenosis of precerebral arteries, multiple and bilateral |
| 04 - PAD | 05 - PAD | PVD | 134472 | Occlusion and stenosis of another precerebral artery |
| 04 - PAD | 05 - PAD | PVD | 134474 | Occlusion and stenosis of a precerebral artery |
| 04 - PAD | 05 - PAD | PVD | 276434 | Carotid artery thrombosis |
| 04 - PAD | 05 - PAD | PVD | 277167 | Bilateral carotid stenosis |
| 04 - PAD | 05 - PAD | PVD | 128726 | Atheroma of the carotid artery |
| 04 - PAD | 05 - PAD | PVD | 269964 | Carotid endarterectomy |
| 04 - PAD | 05 - PAD | PVD | 277167 | Bilateral carotid stenosis |
| 04 - PAD | 05 - PAD | PVD | 128736 | Carotid thromboendarterectomy |
| 04 - PAD | 05 - PAD | PVD | 128789 | Carotid atherosclerosis |
| 04 - PAD | 05 - PAD | PVD | 128833 | Unblocking of the carotid artery |
| 04 - PAD | 05 - PAD | PVD | 133762 | Unblocking of the carotid artery |
| 04 - PAD | 05 - PAD | PVD | 134468 | Occlusion and stenosis of the carotid artery |
| 04 - PAD | 05 - PAD | PVD | 134468 | Occlusion and stenosis of the carotid artery |
| 04 - PAD | 05 - PAD | PVD | 143502 | Angioplasty of a carotid artery |
| 04 - PAD | 05 - PAD | PVD | 143655 | Carotid stenosis |
| 04 - PAD | 05 - PAD | PVD | 269925 | Arterial thrombosis of the lower extremity |
| 04 - PAD | 05 - PAD | PVD | 128834 | Acute ischemia of the lower |

| | | | | |
|---|---|---|---|---|
| | | | | extremity |
| 04 - PAD | 05 - PAD | PVD | 128887 | Acute ischemia of the upper extremity |
| 04 - PAD | 05 - PAD | PVD | 128832 | Arterial embolism of a lower extremity |
| 04 - PAD | 05 - PAD | PVD | 136255 | Arterial embolism of the lower extremities |
| 04 - PAD | 05 - PAD | PVD | 153616 | Distal arterial embolism |
| 04 - PAD | 05 - PAD | PVD | 277259 | Arterial dilatation of the lower extremity with stent |
| 04 - PAD | 05 - PAD | PVD | 128377 | Angioplasty |
| 04 - PAD | 05 - PAD | PVD | 128828 | Angioplasty of the peripheral arteries |
| 04 - PAD | 05 - PAD | PVD | 143315 | Angioplasty |
| 04 - PAD | 05 - PAD | PVD | 143503 | Angioplasty of a peripheral artery |
| 04 - PAD | 05 - PAD | PVD | 143504 | Angioplasty of a renal artery |
| 04 - PAD | 05 - PAD | PVD | 276652 | Iliac angioplasty |
| 04 - PAD | 05 - PAD | PVD | 275998 | Bypass |
| 04 - PAD | 05 - PAD | PVD | 277172 | Arterial stent |
| 04 - PAD | 05 - PAD | PVD | 143504 | Angioplasty of a renal artery |
| 04 - PAD | 05 - PAD | PVD | 277171 | Renal artery stent |
| 04 - PAD | 05 - PAD | PVD | 276109 | Arterial stent |
| 04 - PAD | 05 - PAD | PVD | 276357 | Arterial restenosis |
| 04 - PAD | 05 - PAD | PVD | 277172 | Arterial stent |
| 04 - PAD | 05 - PAD | PVD | 143328 | Endarterectomy |
| 04 - PAD | 05 - PAD | PVD | 128380 | Arteriectomy |
| 04 - PAD | 05 - PAD | PVD | 128383 | Thrombo-endarteriectomy |
| 04 - PAD | 05 - PAD | PVD | 128395 | Arterial prosthesis |
| 04 - PAD | 05 - PAD | PVD | 143314 | Aneurysmectomy |
| 04 - PAD | 05 - PAD | PVD | 277170 | Intra-stent stenosis |
| 04 - PAD | 05 - PAD | PVD | 277173 | Iliac stent |
| 04 - PAD | 05 - PAD | PVD | 277259 | Arterial dilatation of the lower extremity with stent |
| 04 - PAD | 05 - PAD | PVD | 269694 | Surgically repaired aortic aneurysm |
| 04 - PAD | 05 - PAD | PVD | 269878 | Aneurysm of the splenic artery |
| 04 - PAD | 05 - PAD | PVD | 128760 | Abdominal aortic aneurysm |

| | | | | |
|---|---|---|---|---|
| 04 - PAD | 05 - PAD | PVD | 128474 | Monitoring of a surgically repaired aneurysm |
| 04 - PAD | 05 - PAD | PVD | 128187 | Aneurysm of the subrenal aorta |
| 04 - PAD | 05 - PAD | PVD | 128193 | Rupture of an abdominal aortic aneurysm |
| 04 - PAD | 05 - PAD | PVD | 128813 | PAD |
| 04 - PAD | 05 - PAD | PVD | 128584 | Lower extremity arteritis - stage I |
| 04 - PAD | 05 - PAD | PVD | 128587 | Lower extremity arteritis - stage II |
| 04 - PAD | 05 - PAD | PVD | 128590 | Lower extremity arteritis - stage III |
| 04 - PAD | 05 - PAD | PVD | 128593 | Lower extremity arteritis - stage IV |
| 04 - PAD | 05 - PAD | PVD | 128716 | PAD |
| 04 - PAD | 05 - PAD | PVD | 128781 | Peripheral arteriopathy |
| 04 - PAD | 05 - PAD | PVD | 138336 | Claudication |
| 04 - PAD | 05 - PAD | PVD | 145382 | Limb claudication |
| 04 - PAD | 05 - PAD | PVD | 145383 | Calf claudication |
| 04 - PAD | 05 - PAD | PVD | 145384 | Thigh claudication |
| 04 - PAD | 05 - PAD | PVD | 150493 | Intermittent claudication |
| 04 - PAD | 05 - PAD | PVD | 151200 | Intermittent claudication |
| 04 - PAD | 05 - PAD | PVD | 181327 | Claudication |
| 04 - PAD | 05 - PAD | PVD | 143633 | Lower extremity arteritis |
| 04 - PAD | 05 - PAD | PVD | 143713 | PAD |
| 04 - PAD | 05 - PAD | PVD | 275517 | Lower extremity arteritis follow-up |
| 04 - PAD | 05 - PAD | PVD | 128193 | Rupture of an abdominal aortic aneurysm |
| 04 - PAD | 05 - PAD | PVD | 128176 | LOWER EXTREMITY ARTERITIS STAGES I AND II **DELETE** |
| 04 - PAD | 05 - PAD | PVD | 128177 | LOWER EXTREMITY ARTERITIS STAGES III AND IV **DELETE** |
| 04 - PAD | 05 - PAD | PVD | 128841 | Arterial ulcer |
| 05 - DM | 07 - DM | DM | 132993 | Type I DM (insulin-dependent) |
| 05 - DM | 07 - DM | DM | 132996 | Type II DM (noninsulin-dependent) |
| 05 - DM | 07 - DM | DM | 132999 | Asymptomatic DM |
| 05 - DM | 07 - DM | DM | 133161 | Insulin-requiring DM |
| 05 - DM | 07 - DM | DM | 143870 | Type 1 DM |
| 05 - DM | 07 - DM | DM | 143871 | Type 2 DM |

| | | | | |
|---|---|---|---|---|
| 05 - DM | 07 - DM | DM | 143908 | DM |
| 05 - DM | 07 - DM | DM | 143951 | Insulin-requiring DM |
| 05 - DM | 07 - DM | DM | 146119 | DM |
| 05 - DM | 07 - DM | DM | 146998 | DM |
| 05 - DM | 07 - DM | DM | 181265 | Type 1 DM - nonidentified |
| 05 - DM | 07 - DM | DM | 275765 | Type 2 DM - nonidentified |
| 05 - DM | 07 - DM | DM | 277325 | Insulin-treated type 2 DM |
| 05 - DM | 07 - DM | DM | 152520 | Monitoring of DM |
| 05 - DM | 07 - DM | DM | 152763 | DM check-up |
| 05 - DM | 07 - DM | DM | 152766 | Education of the diabetic patient |
| 05 - DM | 07 - DM | DM | 276069 | Diabetic dermatitis |
| 05 - DM | 07 - DM | DM | 276057 | Decompensated diabetic ketoacidosis |
| 05 - DM | 07 - DM | DM | 143943 | Type 1 DM with multiple complications |
| 05 - DM | 07 - DM | DM | 143944 | Type 1 DM complicated by nephropathy |
| 05 - DM | 07 - DM | DM | 143945 | Type 1 DM complicated by neuropathy |
| 05 - DM | 07 - DM | DM | 143946 | Type 1 DM complicated by retinopathy |
| 05 - DM | 07 - DM | DM | 143947 | Type 2 DM with multiple complications |
| 05 - DM | 07 - DM | DM | 143948 | Type 2 DM complicated by nephropathy |
| 05 - DM | 07 - DM | DM | 143949 | Type 2 DM complicated by neuropathy |
| 05 - DM | 07 - DM | DM | 143950 | Type 2 DM complicated by retinopathy |
| 05 - DM | 07 - DM | DM | 133005 | Chronic complications of diabetes |
| 05 - DM | 07 - DM | DM | 139484 | Glomerulonephritis related to DM |
| 05 - DM | 07 - DM | DM | 276074 | Decompensated DM |
| 05 - DM | 07 - DM | DM | 129212 | Diabetic malum perforans |
| 05 - DM | 07 - DM | DM | 133105 | Coma in the diabetic patient |
| 05 - DM | 07 - DM | DM | 133196 | Diabetic ketoacidosis |
| 05 - DM | 07 - DM | DM | 133651 | Diabetic neuropathy |
| 05 - DM | 07 - DM | DM | 134661 | Diabetic mononeuritis |
| 05 - DM | 07 - DM | DM | 134711 | Diabetic polyneuritis |

| | | | | |
|---|---|---|---|---|
| 05 - DM | 07 - DM | DM | 135471 | Diabetic cataract |
| 05 - DM | 07 - DM | DM | 135479 | Diabetic retinopathy |
| 05 - DM | 07 - DM | DM | 138194 | Diabetic arthropathy |
| 05 - DM | 07 - DM | DM | 139870 | Diabetic nephropathy |
| 05 - DM | 07 - DM | DM | 140129 | Confusional state due to diabetic ketoacidosis |
| 05 - DM | 07 - DM | DM | 141591 | Diabetic arthropathy |
| 05 - DM | 07 - DM | DM | 143197 | Diabetic gastroparesis |
| 05 - DM | 07 - DM | DM | 144219 | Diabetic mononeuritis |
| 05 - DM | 07 - DM | DM | 144223 | Diabetic polyneuritis |
| 05 - DM | 07 - DM | DM | 144245 | Diabetic neuropathy |
| 05 - DM | 07 - DM | DM | 144444 | Diabetic retinopathy |
| 05 - DM | 07 - DM | DM | 133011 | Diabetic coma |
| 05 - DM | 07 - DM | DM | 139913 | Incipient nephropathy (DM) |

ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; MI = myocardial infarction; PVD = peripheral vascular disease.

**Supplementary Table II. Statin dose categories for France and UK cross-country comparisons.**

| Statin intensity | France | UK (NICE 2014 [1]) |
|---|---|---|
| **High** | Atorvastatin 40, 60, and 80 mg<br>Rosuvastatin 20 and 40 mg<br>Simvastatin 80 mg | Atorvastatin 20, 40, 60, and 80 mg<br>Rosuvastatin 10, 20, and 40 mg<br>Simvastatin 80 mg |
| **Moderate/low** | Atorvastatin 10, 20, and 30 mg<br>Rosuvastatin 5 and 10 mg<br>Simvastatin 10, 20, and 40 mg<br>Pravastatin 10, 20, and 40 mg<br>Fluvastatin 20, 40, and 80 mg | N/A |
| **Medium** | N/A | Atorvastatin 10 mg<br>Rosuvastatin 5 mg<br>Simvastatin 20 and 40 mg<br>Fluvastatin 80 mg |
| **Low** | N/A | Simvastatin 10 mg<br>Pravastatin 10, 20, and 40 mg<br>Fluvastatin 20 and 40 mg |

N/A = not applicable.

1. National Institute for Health and Care Excellence. Cardiovascular disease: risk assessment and reduction, including lipid modification. 2014. Available at http://www.nice.org.uk/guidance/cg181.

**Supplementary Table III. Patient characteristics for the overall study cohort and prevalent disease categories.**

| | Total cohort N = 32,924 | Recent ACS n =293 | Chronic CHD n = 10,469 | Ischemic stroke/TIA n = 2763 | PAD n = 6068 | DM n = 21,040 |
|---|---|---|---|---|---|---|
| **Demographics** | | | | | | |
| Age, mean (SD) | 68.3 (12.2) | 64.2 (14.1) | 70.9 (11.8) | 70.5 (12.7) | 71.9 (11.1) | 67.1 (11.8) |
| Male, % | 58.9 | 73.7 | 69.5 | 55.2 | 67.6 | 56.3 |
| **Cardiovascular risk conditions, %** | | | | | | |
| Recent ACS | 0.9 | 100 | 2.4 | 0.4 | 0.5 | 0 |
| Chronic CHD | 31.8 | 87.4 | 100 | 15.8 | 27.7 | 0 |
| Ischemic stroke/TIA | 8.4 | 3.8 | 4.2 | 100 | 6.0 | 3.4 |
| PAD | 18.4 | 10.2 | 16.1 | 13.1 | 100 | 9.2 |
| DM | 63.9 | 17.7 | 31.6 | 26.2 | 32.0 | 100 |
| **Behaviors and comorbidities of interest, %** | | | | | | |
| Current smokers, % | 8.1 | 14.3 | 8.5 | 7.6 | 14.1 | 7.2 |
| Hypertension | 67.6 | 45.1 | 63.8 | 68.9 | 72.5 | 71.2 |
| History of CHF[a] | 3.6 | 2.7 | 6.7 | 3.7 | 4.5 | 3.2 |
| CKD | 1.9 | 1.4 | 2.4 | 2.6 | 3.6 | 1.9 |
| Stage V[b] | 0.2 | 0 | 0.2 | 0.2 | 0.2 | 0.2 |
| Dementia[a] | 0.5 | 0.3 | 0.5 | 1.1 | 0.6 | 0.4 |
| COPD[a] | 10.1 | 9.6 | 12.8 | 9.6 | 18.5 | 8.7 |
| Diagnosis associated with musculoskeletal pain | 87.4 | 86.7 | 88.9 | 86.9 | 90.1 | 86.8 |
| Moderate/severe liver disease[a] | 0.3 | 0 | 0.1 | 0.1 | 0.3 | 0.4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Concomitant medications, %** | | | | | | |
| Beta-blockers | 44.9 | 77.8 | 71.4 | 41.1 | 44.6 | 40.0 |
| ACEIs/ARBs | 65.8 | 74.4 | 72.9 | 67.6 | 68.9 | 66.7 |
| Clopidogrel | 19.3 | 20.8 | 37.8 | 27.0 | 41.0 | 12.0 |

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; N/A = not applicable; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

[a]Based on Quan-Charlson comorbidity scale components.

[b]Stage V includes end-stage renal disease and dialysis.

**Supplementary Table IV. Comparison of baseline characteristics for those with and without a LDL-C measurement in 2015 using hierarchical classification.**

| | Combined ASCVD and/or DM | | ASCVD | | DM | |
|---|---|---|---|---|---|---|
| | With LDL-C measurement (n = 32,924) | Without LDL-C measurement (n = 100,254) | With LDL-C measurement (n = 16,962) | Without LDL-C measurement (n = 52,574) | With LDL-C measurement (n = 15,962) | Without LDL-C measurement (n = 47,680) |
| **Demographics** | | | | | | |
| Age, mean (SD) | 68.3 (12.2) | 66.7 (14.7) | 70.7 (11.9) | 69.0 (14.9) | 65.8 (11.9) | 64.2 (14.1) |
| Male, % | 58.9 | 56.4 | 65.4 | 62.0 | 52.0 | 50.3 |
| **Cardiovascular risk conditions, %** | | | | | | |
| Recent ACS | 0.9 | 0.9 | 1.7 | 1.7 | 0 | 0 |
| Chronic CHD | 31.8 | 32.5 | 61.7 | 61.6 | 0 | 0 |
| Ischemic stroke/TIA | 8.4 | 8.9 | 16.3 | 16.0 | 0 | 0 |
| PAD | 18.4 | 16.6 | 35.8 | 32.9 | 0 | 0 |
| DM | 63.9 | 59.5 | 29.9 | 22.8 | 100 | 100 |
| **Comorbidities of interest, %** | | | | | | |
| Hypertension | 67.6 | 60.9 | 66.2 | 59.9 | 69.2 | 62.2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| History of CHF[a] | 3.6 | 3.8 | 5.2 | 5.5 | 2.0 | 2.0 |
| CKD | 1.9 | 1.9 | 2.4 | 2.5 | 1.3 | 1.4 |
| Stage V[b] | 0.2 | 0.3 | 0.2 | 0.4 | 0.1 | 0.2 |
| Dementia[a] | 0.5 | 0.7 | 0.6 | 0.8 | 0.4 | 0.5 |
| COPD[a] | 10.1 | 9.6 | 13.2 | 12.3 | 6.9 | 6.7 |
| Diagnosis associated with musculoskeletal pain | 87.4 | 81.9 | 88.7 | 83.4 | 86.0 | 80.2 |
| Moderate/severe liver disease[a] | 0.3 | 0.2 | 0.2 | 0.2 | 0.4 | 0.3 |
| **Concomitant medications, %** | | | | | | |
| Beta-blockers | 44.9 | 41.0 | 56.7 | 51.6 | 32.3 | 29.1 |
| ACEIs/ARBs | 65.8 | 59.2 | 69.4 | 61.9 | 61.9 | 56.2 |
| Clopidogrel | 19.3 | 17.8 | 34.4 | 30.9 | 3.3 | 3.5 |

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; ASCVD = atherosclerotic cardiovascular disease; CHD, coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

[a]Based on Quan-Charlson comorbidity scale components.

[b]Stage V includes end-stage renal disease and dialysis.

The final study cohort was compared to another cohort from the same database who met the all the inclusion criteria, except presence of a valid LDL-C measurement in 2015 to ensure the generalizability of the study population. Compared with the population without a valid LDL-C measurement, those for whom a LDL-C measurement was available were 1.5 years older and 2% more males. Although differences were statistically significant due to large numbers, most were small and not of clinical importance. Patients prescribed beta-blockers, ACE inhibitors, ARBs, and clopidogrel were more likely to have had an LDL-C measurement.

**Supplementary Table V. Comparison of baseline characteristics according to statin therapy.**

| | ASCVD | | | | DM | | | |
|---|---|---|---|---|---|---|---|---|
| | **High-intensity statin** | **Low-to-moderate-intensity statin** | **Any current statin** | **No current statin** | **High-intensity statin** | **Low-to-moderate-intensity statin** | **Any current statin** | **No current statin** |
| **Demographics** | | | | | | | | |
| Age, mean (SD) | 68.9 (11.3) | 71.8 (10.6) | 70.7 (10.9) | 70.7 (13.0) | 66.5 (10.3) | 67.3 (10.6) | 67.1 (10.6) | 65.0 (12.7) |
| Male, % | 74.7 | 67.4 | 70.1 | 59.5 | 57.0 | 53.0 | 53.8 | 50.9 |
| **Cardiovascular risk conditions, %** | | | | | | | | |
| Recent ACS | 4.3 | 1.1 | 2.3 | 1.0 | – | – | – | – |
| Chronic CHD | 75.0 | 61.0 | 66.3 | 56.0 | – | – | – | – |
| Ischemic stroke/TIA | 15.7 | 14.9 | 15.2 | 17.7 | – | – | – | – |
| PAD | 27.3 | 39.2 | 34.7 | 37.1 | – | – | – | – |
| DM | 31.3 | 33.7 | 32.8 | 26.3 | 100 | 100 | 100 | 100 |
| **Comorbidities of interest, %** | | | | | | | | |
| Hypertension | 63.4 | 71.0 | 68.2 | 63.8 | 77.2 | 77.8 | 77.7 | 63.7 |
| History of CHF[a] | 5.5 | 5.0 | 5.2 | 5.1 | 2.6 | 2.2 | 2.2 | 1.9 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CKD | 1.9 | 2.6 | 2.4 | 2.5 | 1.8 | 1.2 | 1.3 | 1.2 |
| Stage IV-V[b] | 0.1 | 0.1 | 0.1 | 0.3 | 0.1 | 0.1 | 0.1 | 0.1 |
| Dementia[a] | 0.3 | 0.6 | 0.5 | 0.7 | 0.3 | 0.3 | 0.3 | 0.4 |
| COPD[a] | 12.7 | 14.3 | 13.7 | 12.5 | 8.9 | 7.5 | 7.8 | 6.3 |
| Diagnosis associated with musculoskeletal pain | 87.4 | 90.7 | 89.5 | 87.7 | 86.6 | 88.1 | 87.8 | 84.9 |
| Moderate/severe liver disease[a] | 0.1 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.5 |
| **Concomitant medications, %** | | | | | | | | |
| Beta-blockers | 73.8 | 59.7 | 65.0 | 46.1 | 40.3 | 36.2 | 37 | 29.4 |
| ACEIs/ARBs | 81.0 | 74.0 | 76.7 | 60.3 | 73.8 | 72.6 | 72.9 | 55.0 |
| Clopidogrel | 45.9 | 39.1 | 41.6 | 25.2 | 7.5 | 4.4 | 5.0 | 2.3 |

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

[a]Based on Quan-Charlson comorbidity scale components.

[b]Stage V includes end-stage renal disease and dialysis.

**Supplementary Table VI. Use of LLT in overall cohort and by prevalent disease categories.**

| | Total cohort N = 32,924 | Recent ACS n = 293 | Chronic CHD n = 10,469 | Ischemic stroke/TIA n = 2763 | PAD n = 6068 | DM n = 21,040 |
|---|---|---|---|---|---|---|
| High-intensity statin | 6.9 | 43.3 | 14.1 | 11.3 | 7.6 | 4.5 |
| Monotherapy | 92.2 | 98.4 | 91.6 | 95.2 | 90.4 | 92.8 |
| Plus ezetimibe | 7.4 | 1.6 | 8.1 | 4.8 | 8.7 | 6.5 |
| Plus fibrate | 0.3 | 0 | 0.2 | 0 | 0.4 | 0.4 |
| Plus other non-statin LLT | 0.1 | 0 | 0.1 | 0 | 0.4 | 0.2 |
| Low-to-moderate-intensity statin | 40.6 | 30.0 | 45.8 | 40.8 | 46.6 | 39.6 |
| Monotherapy | 89.3 | 95.5 | 84.6 | 92.2 | 88.5 | 90.6 |
| Plus ezetimibe | 10.1 | 4.5 | 14.8 | 7.5 | 10.8 | 8.5 |
| Plus fibrate | 0.1 | 0 | 0.1 | 0.2 | 0.1 | 0.2 |
| Plus other non-statin LLT | 0.6 | 0 | 0.5 | 0.1 | 0.6 | 0.7 |
| Non-statin LLT only | 4.8 | 1.7 | 3.8 | 3.5 | 4.5 | 5.2 |
| Ezetimibe | 24.4 | 60.0 | 44.3 | 22.7 | 31.8 | 18.4 |
| Fibrate | 74.6 | 40.0 | 53.7 | 75.3 | 66.4 | 80.7 |
| Other non-statin LLT | 1.0 | 0 | 2.0 | 2.1 | 1.8 | 0.9 |
| Evidence of prior LLT | 22.5 | 14.7 | 23.7 | 22.6 | 24.4 | 22.1 |
| High-intensity statin | 29.0 | 58.1 | 43.1 | 37.4 | 32.7 | 25.5 |
| Low-to-moderate-intensity statin | 57.9 | 41.9 | 50.6 | 54.0 | 60.6 | 64.2 |
| Non-statin LLT | 9.5 | 0 | 6.3 | 8.6 | 6.7 | 11.3 |
| No evidence of prior LLT | 25.2 | 10.2 | 12.6 | 21.8 | 16.9 | 28.6 |

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Numbers in the gray bars denote absolute percentages. They add up to 100% when added vertically for each column. Numbers in the white bars are relative percentages of the absolute percentages in the gray bars. Subcategories in the white bars are hierarchical. ASCVD subgroups represent prevalent categorization.

**Supplementary Table VII. Mean LDL-C and non-HDL-C levels and threshold achievement in hierarchical disease categories.**

| | Total cohort N = 32,924 | Recent ACS n = 293 | Chronic CHD n = 10,213 | Ischemic stroke/TIA n = 2324 | PAD n = 4132 | DM n = 15,962 |
|---|---|---|---|---|---|---|
| LDL-C | | | | | | |
| Mean (±SD), mmol/l | 2.7 (1.0) | 2.2 (0.9) | 2.5 (1.0) | 2.7 (1.0) | 2.8 (1.0) | 2.8 (1.0) |
| <1.8 mmol/l, % | 12.3 | 29.0 | 15.7 | 12.3 | 9.5 | 10.7 |
| 1.8–<2.5 mmol/l, % | 33.6 | 41.6 | 39.5 | 35.2 | 29.8 | 30.5 |
| 2.5–<3.4 mmol/l, % | 33.8 | 20.5 | 28.7 | 32.1 | 36.6 | 36.8 |
| 3.4–<4.1 mmol/l, % | 13.9 | 4.8 | 10.9 | 13.3 | 16.6 | 15.4 |
| ≥4.1 mmol/l, % | 6.3 | 4.1 | 5.1 | 7.1 | 7.5 | 6.7 |
| Non-HDL-C[a] | | | | | | |
| Mean (±SD), mmol/l | 3.4 (1.1) | 2.8 (1.0) | 3.2 (1.0) | 3.3 (1.1) | 3.5 (1.1) | 3.5 (1.0) |
| <2.6 mmol/l, % | 21.1 | 41.6 | 28.4 | 25.0 | 18.0 | 16.3 |
| 2.6–<3.3 mmol/l, % | 25 | 25.6 | 27.6 | 24.2 | 23.8 | 23.6 |
| 3.3–<4.1 mmol/l, % | 23.3 | 14.7 | 19.6 | 22.4 | 25.0 | 25.5 |
| 4.1–<4.9 mmol/l, % | 13 | 5.8 | 10.1 | 12.3 | 14.3 | 14.8 |
| ≥4.9 mmol/l, % | 7.5 | 3.8 | 6.1 | 7.1 | 9.1 | 8.0 |

ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

[a]Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data.

**Supplementary Table VIII. Comparison of LLT between French and UK [1] study populations by hierarchical disease categories.**

| | Recent ACS | | Chronic CHD | | Ischemic stroke/TIA | | PAD | | DM | |
|---|---|---|---|---|---|---|---|---|---|---|
| | UK (n = 3386) | France (n = 293) | UK (n = 63,387) | France (n = 10,213) | UK (n = 2614) | France (n = 2324) | UK (n = 12,854) | France (n = 4132) | UK[a] (n = 56,962) | France (n = 15,962) |
| **High-dose statin** | 62.4 | 51.5 | 34.6 | 24.7 | 21.5 | 18.3 | 23.2 | 11.0 | 18.7 | 7.2 |
| Monotherapy | 93.3 | 98.7 | 91.8 | 92.9 | 93.2 | 96.5 | 92.3 | 95.4 | 92.0 | 95.9 |
| Plus ezetimibe | 1.0 | 1.3 | 4.8 | 6.9 | 2.9 | 3.5 | 3.4 | 4.0 | 2.6 | 3.4 |
| **Moderate-dose statin** | 22.6 | 15.4 | 41.4 | 24.2 | 46.2 | 21.9 | 44.3 | 24.9 | 42.6 | 20.6 |
| Monotherapy | 98.6 | 91.1 | 97.9 | 75.4 | 98.7 | 89.6 | 98.6 | 86.2 | 98.2 | 86.7 |
| Plus ezetimibe | 0.6 | 8.9 | 1.2 | 23.7 | 0.7 | 10.0 | 0.6 | 12.7 | 0.8 | 12.0 |
| **Low-dose statin** | 2.1 | 6.5 | 5.9 | 10.6 | 5.5 | 9.5 | 5.1 | 13.1 | 4.8 | 11.0 |
| Monotherapy | 93.8 | 100 | 95.9 | 93.5 | 97.4 | 97.7 | 97.1 | 98.7 | 96.1 | 98.6 |
| Plus ezetimibe | 6.3 | 0 | 3.2 | 6.3 | 1.7 | 1.8 | 2.3 | 1.3 | 0.9 | 1.2 |
| **Non-statin only** | 0.9 | 1.7 | 2.0 | 3.8 | 1.7 | 3.7 | 1.9 | 5.1 | 1.7 | 5.5 |
| Ezetimibe, monotherapy | 70.4 | 60.0 | 61.3 | 44.1 | 65.5 | 22.4 | 55.6 | 28.9 | 63.4 | 14.5 |
| **No evidence of prior LLT** | 5.6 | 10.2 | 4.1 | 12.7 | 10.5 | 24.2 | 12.0 | 22.4 | 22.1 | 34.3 |

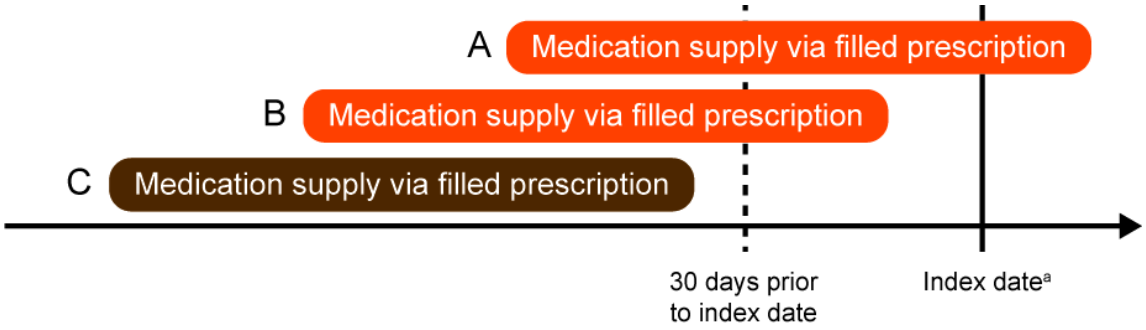
ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Data are percentages. French data re-analyzed according to the UK statin dose definition.

[a]UK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population [1].

1. Steen DL, Khan I, Ansell D, et al. Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK in 2014: Comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. BMJ Open 7 (2017) e013255.

**Supplementary Figure 1. Determination of treatment status as of the index date.**



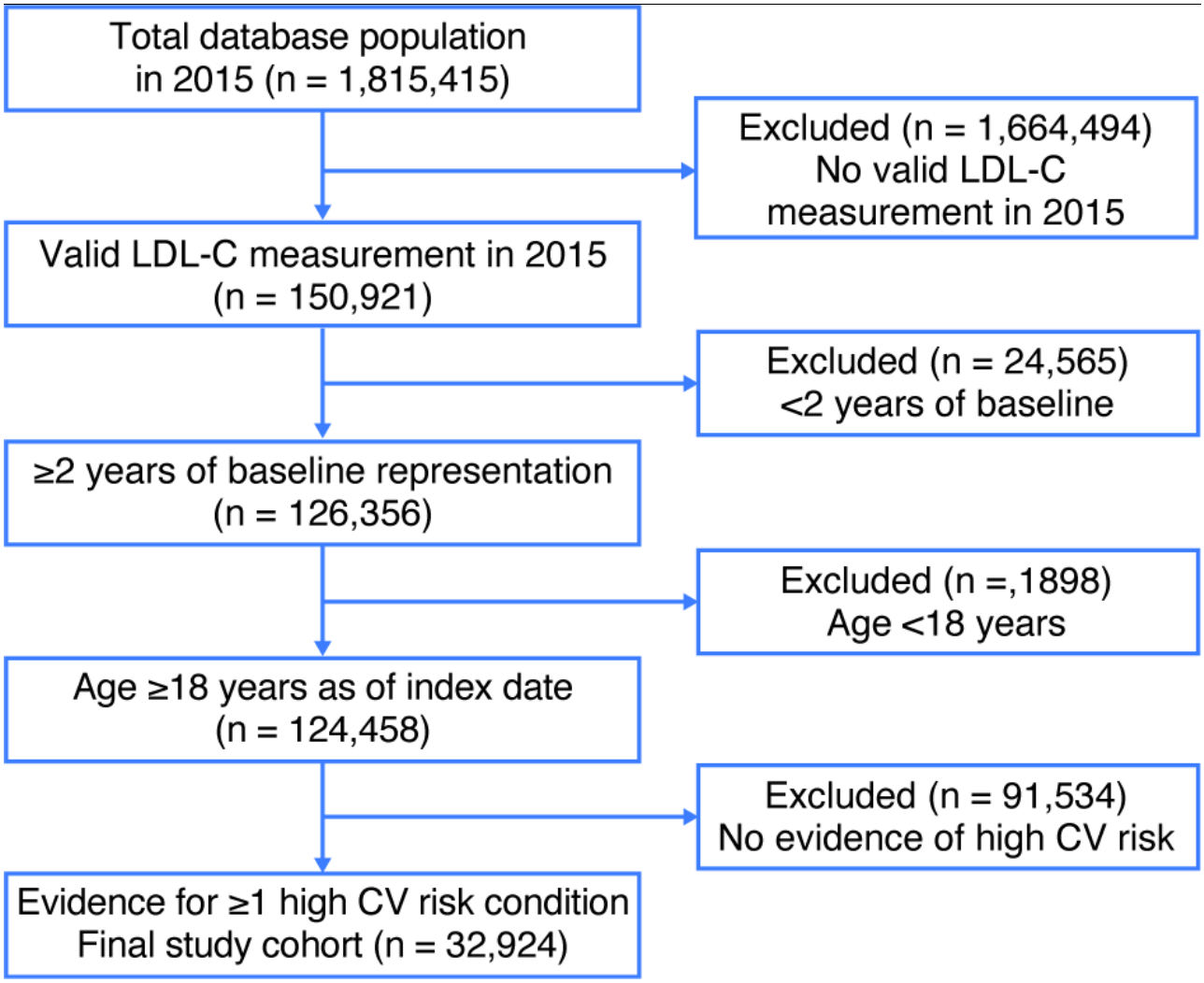

LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy.

[a] Defined as the last LDL-C measurement in 2015.

Reproduced with permission from Steen et al. *Clinical Cardiology* 40 (2017): 155-162,

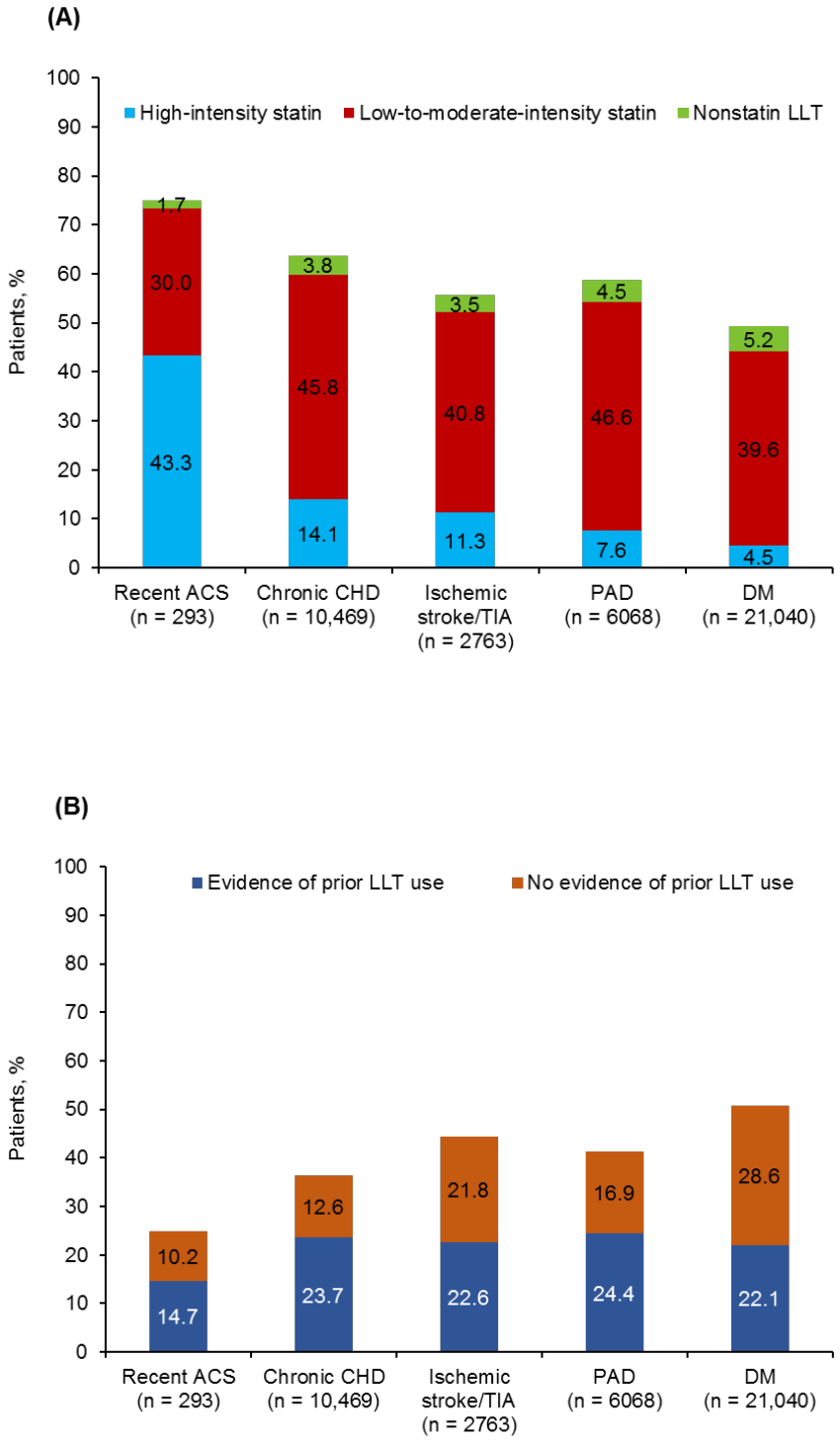
Orange bars (A and B) denote scenarios whereby a patient is deemed to be currently treated with LLT as of the index date, since there is (A) evidence of medication supply (established via recorded prescription) on, or (B) within 30 days of index date. The brown bar (C) denotes a scenario whereby the patient is not being deemed as currently treated as of the index date, since there is no evidence of medication supply within 30 days before the index date.

**Supplementary Figure 2. Cohort selection.**



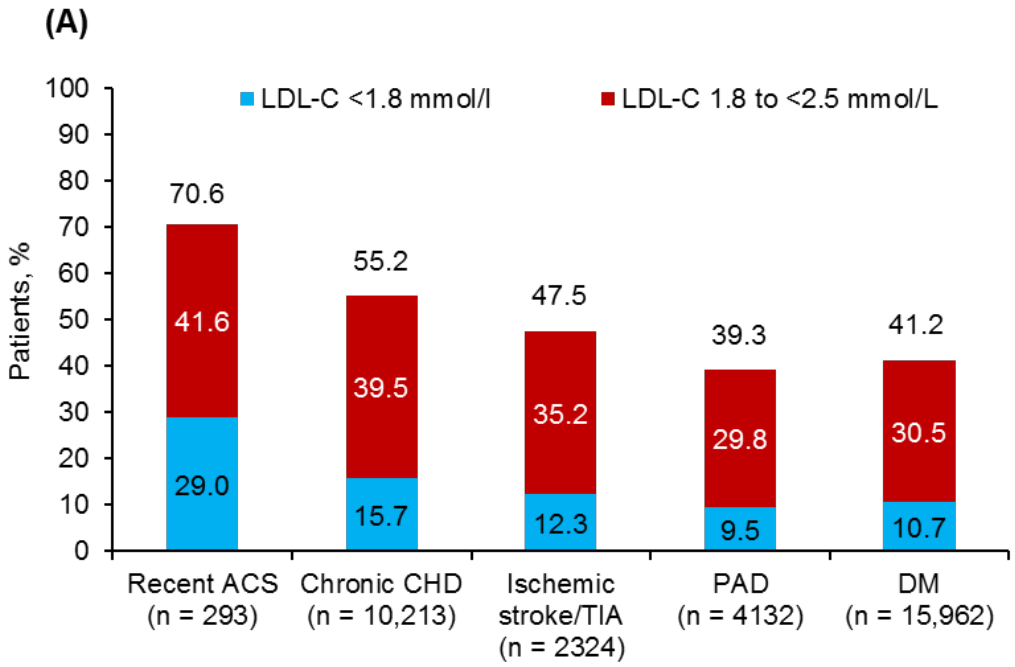

CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol.

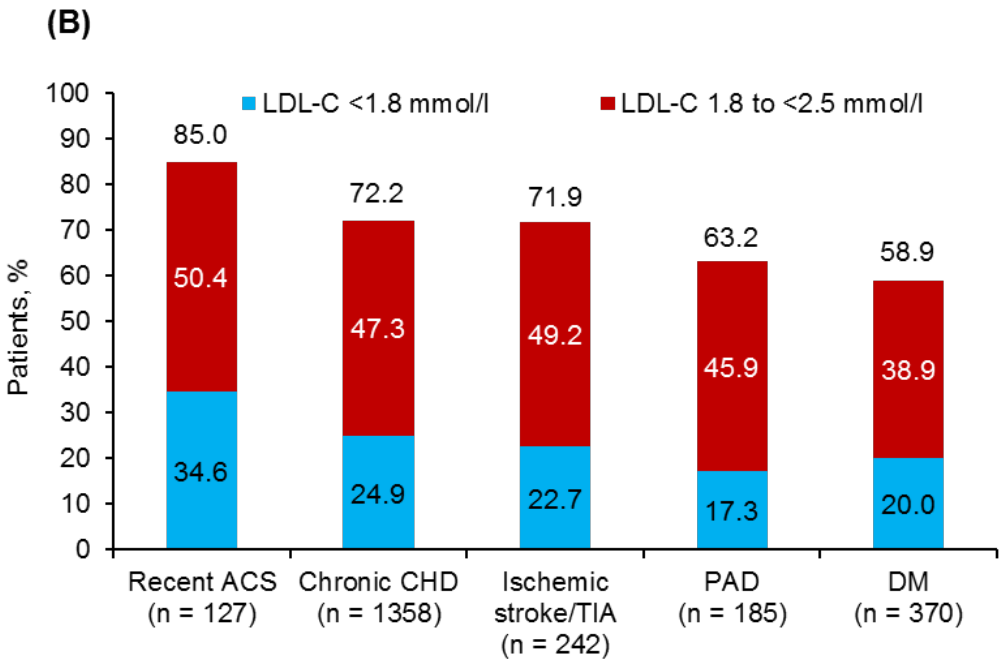
**Supplementary Figure 3. Absolute proportions of (A) patients currently treated and (B) not currently treated, by prevalent disease categories.**

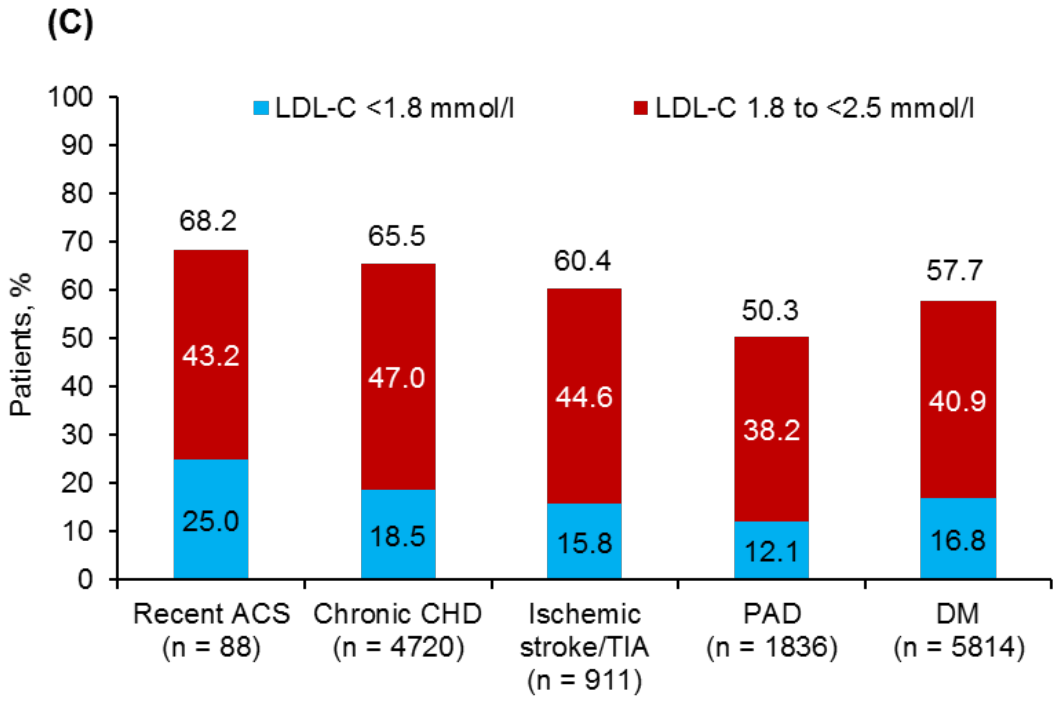



ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

**Supplementary Figure 4. Subgroup analyses of LDL-C goal achievement by hierarchical disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.**

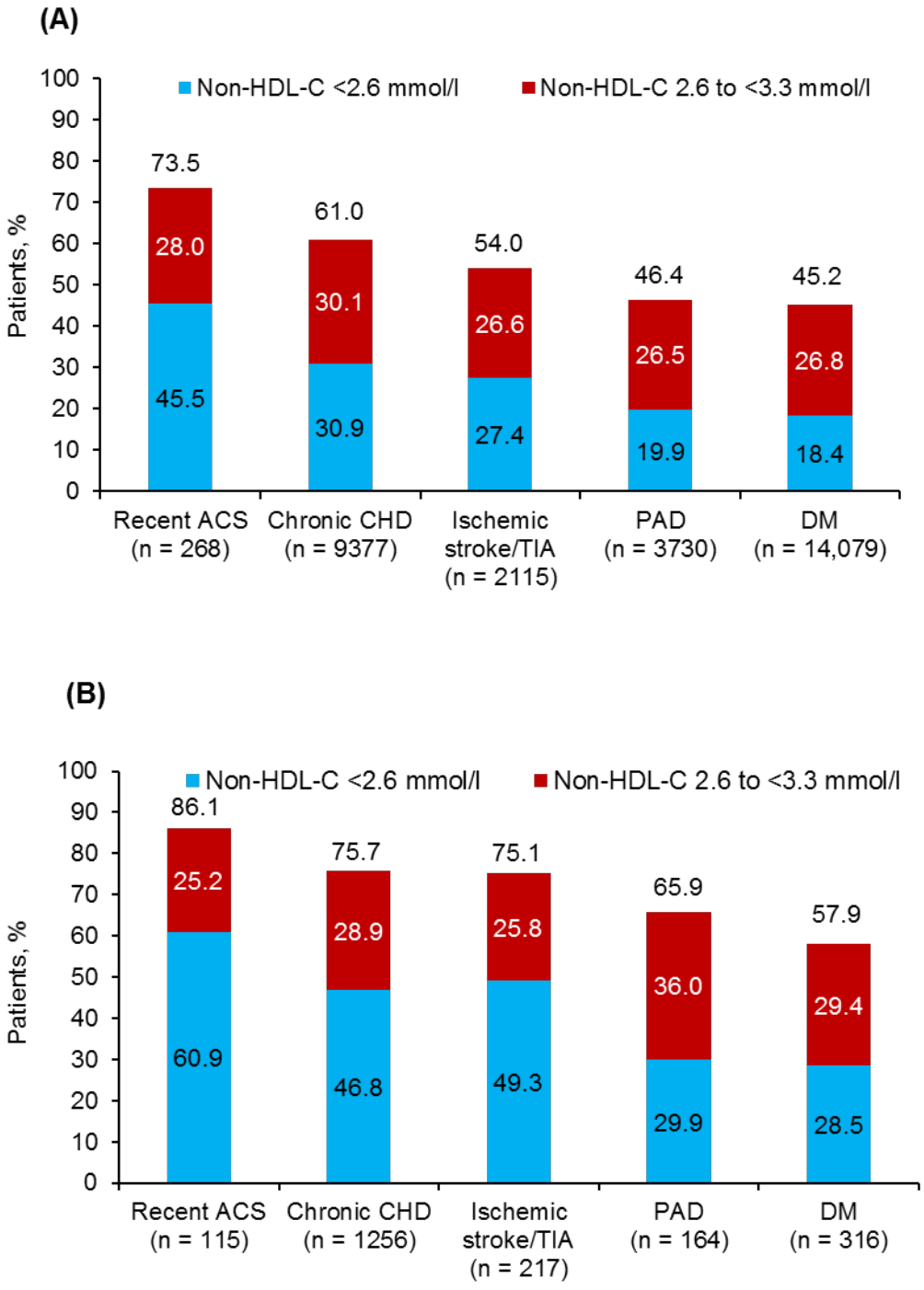


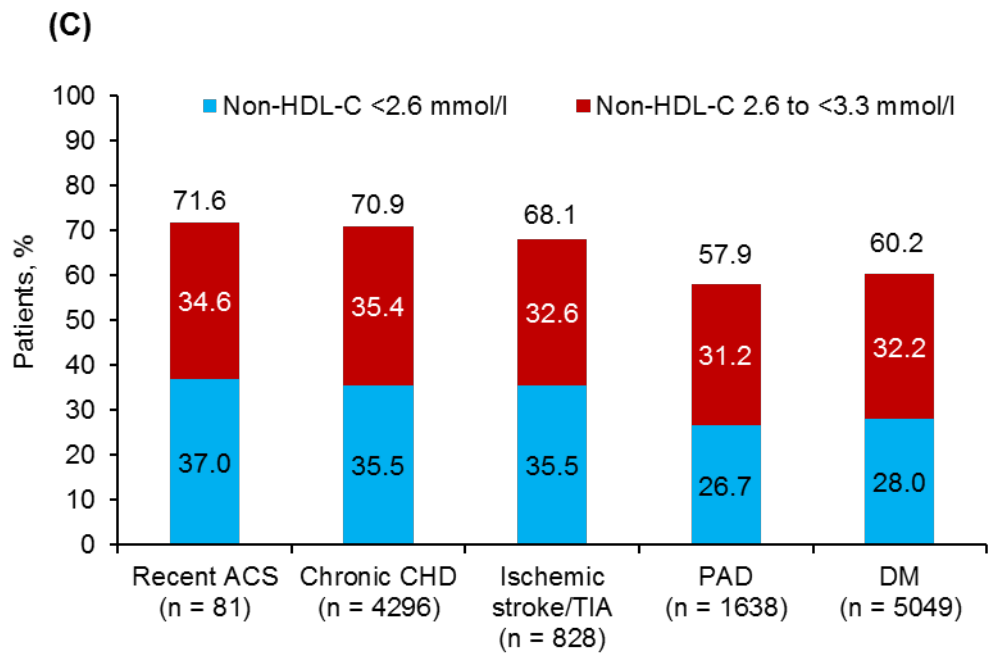






ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.

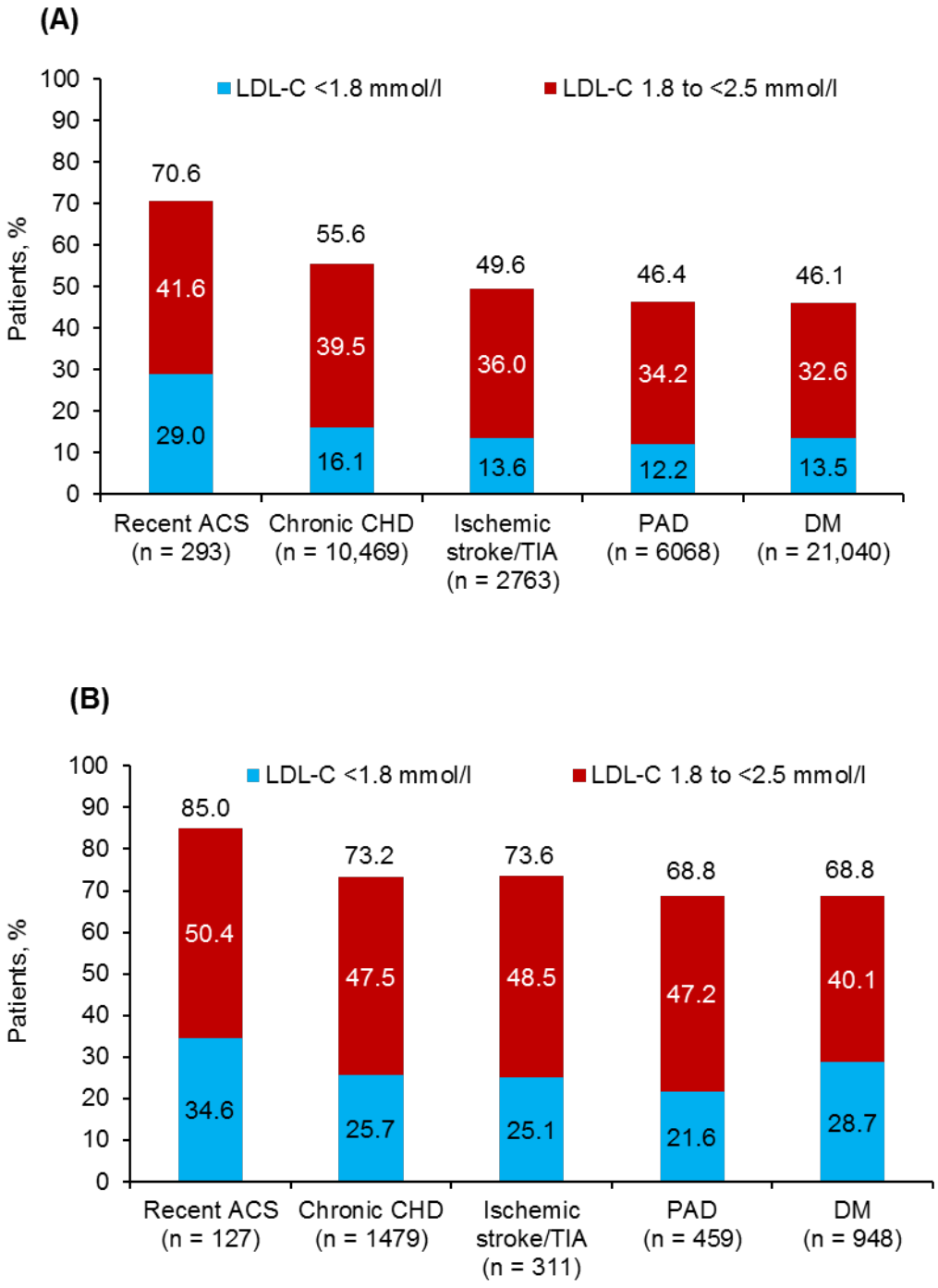
**Supplementary Figure 5. Subgroup analyses of non-HDL-C goal achievement by hierarchical disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.**



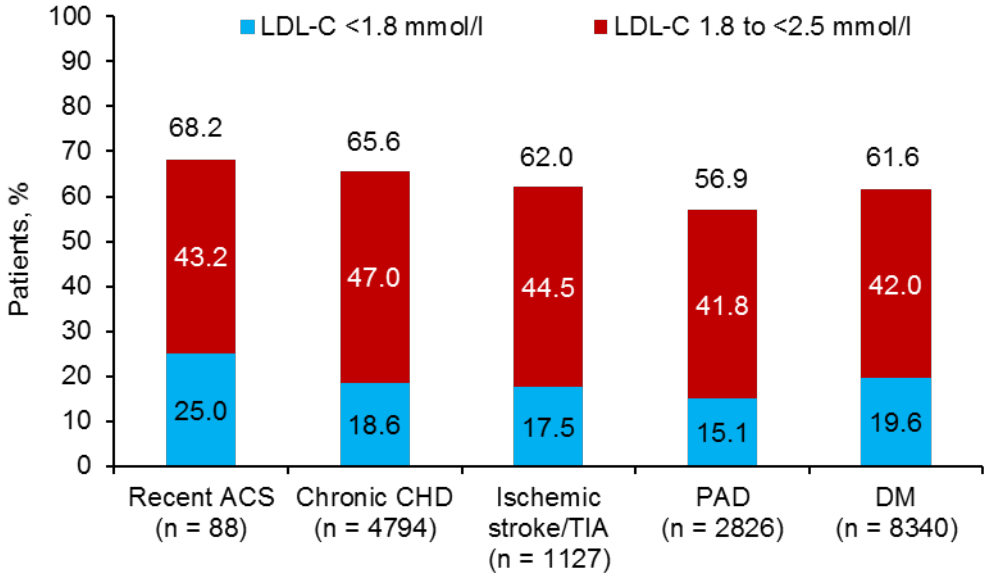



Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data. ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.

**Supplementary Figure 6. Subgroups of LDL-C goal achievement by prevalent disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.**

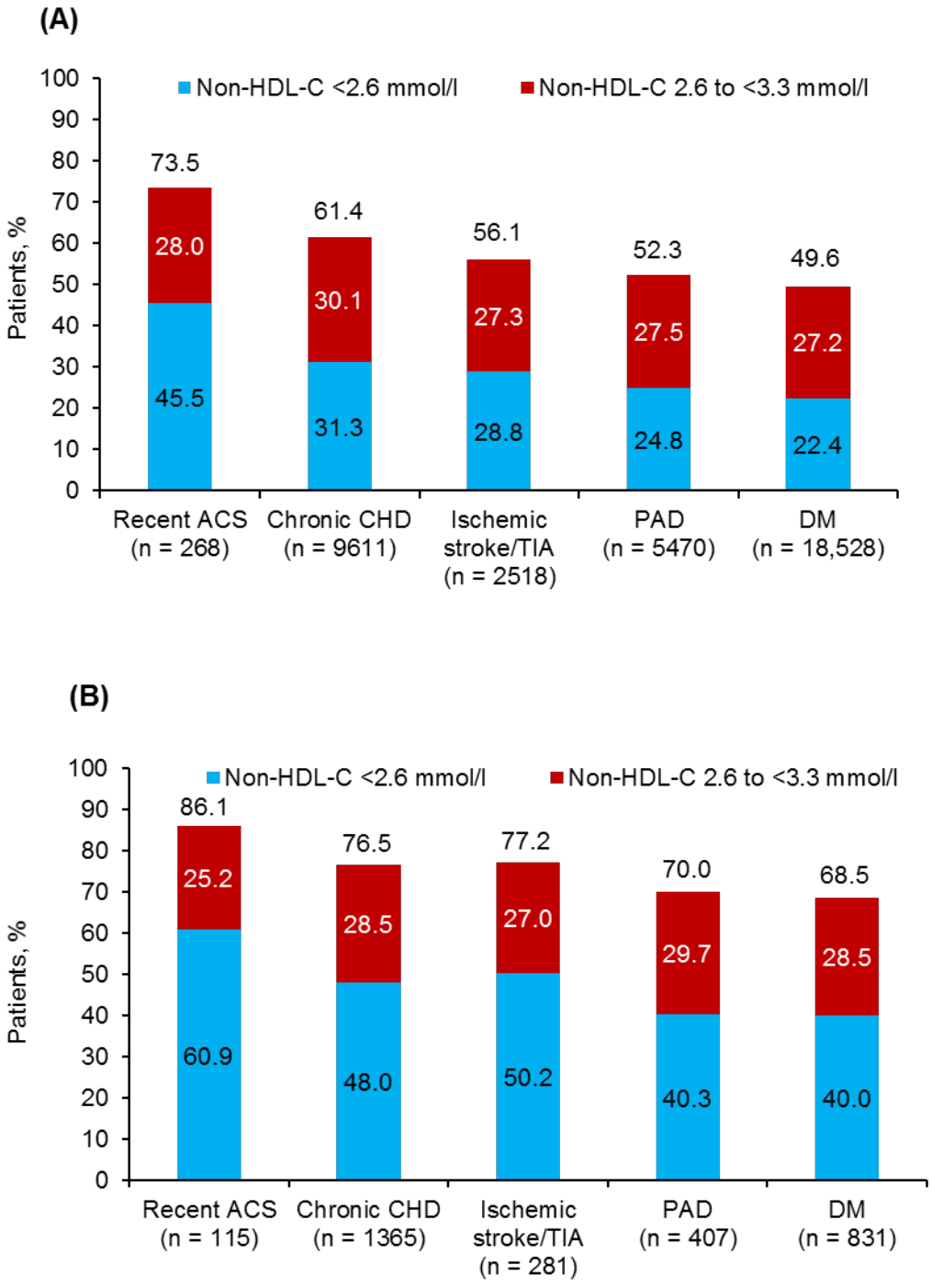


**(C)**

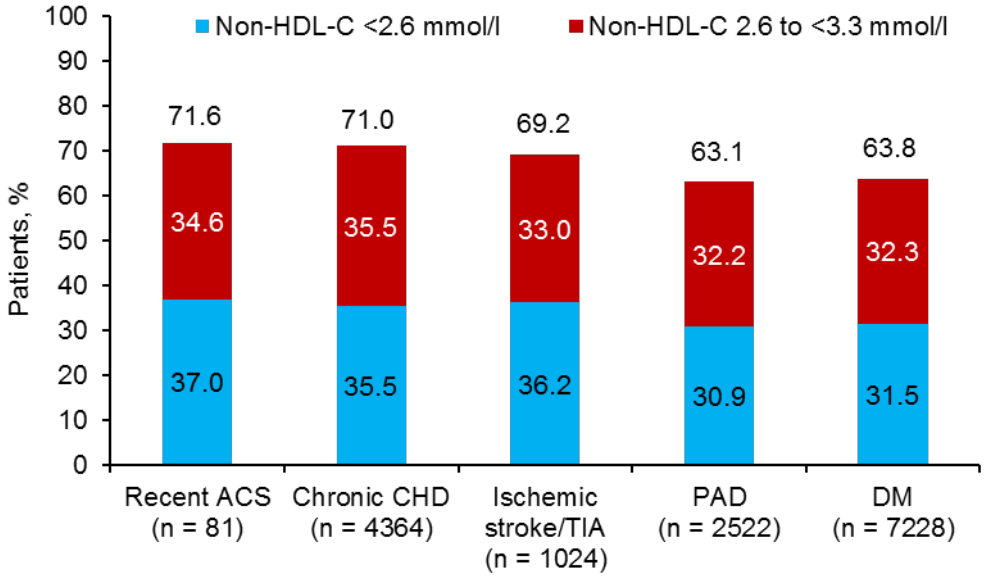



ACS = acute coronary syndrome; CHD = coronary heart disease; DM =, diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack

**Supplementary Figure 7. Subgroups of non-HDL-C goal achievement by prevalent disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.**



**(C)**




Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data. ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.